EXPÉRIMENTATION ANIMALE

Projet **ALGOMENU**

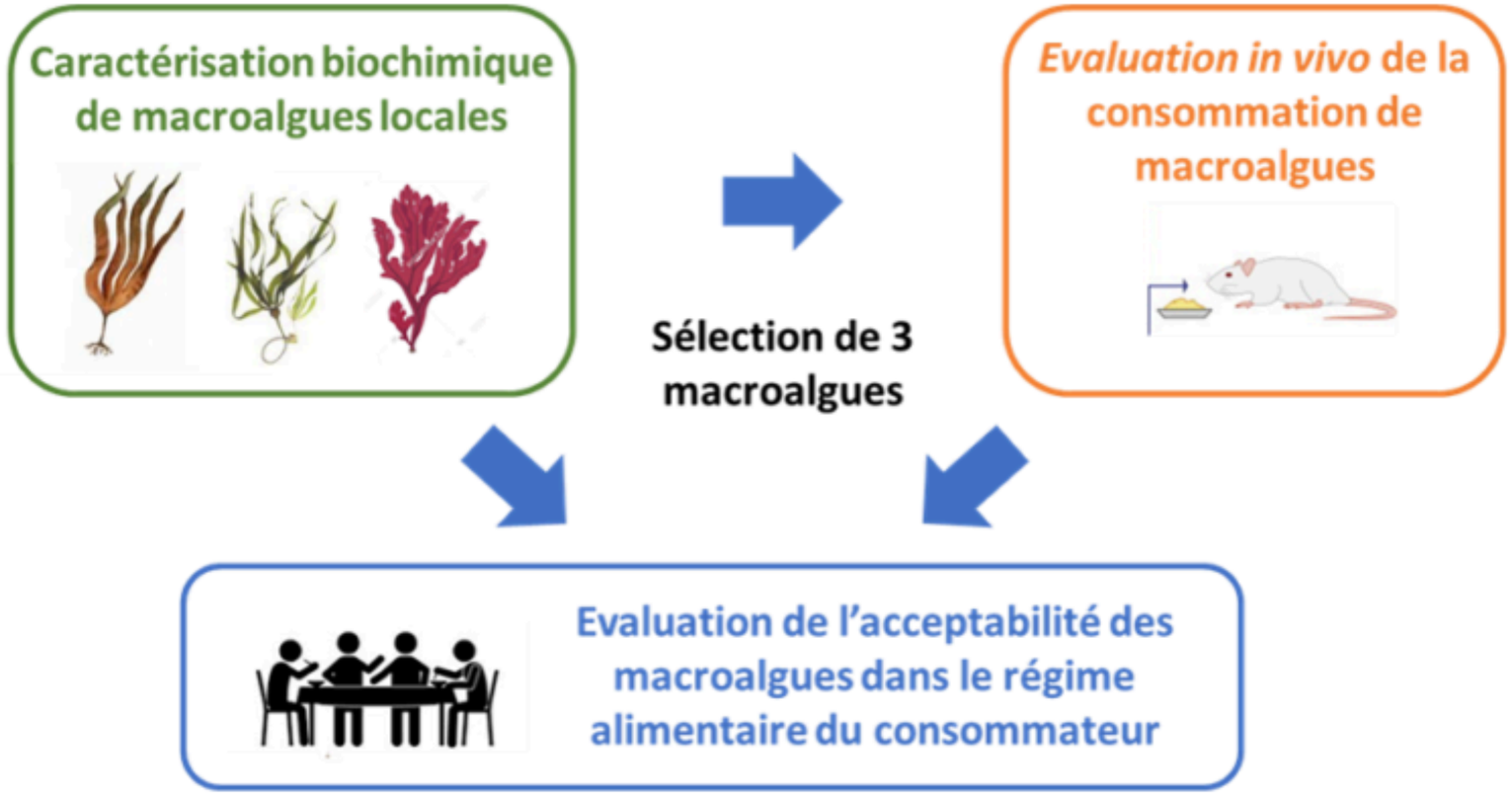
Gaëlle BOUDRY, Anne CORLU, Annaïg LAN, Olivier LORÉAL
Elise GIERYGA, Régis JANVIER, Patricia LEROYER, Gwénaëlle RANDUINEAU

Présentation pôle EA

25/09/2026

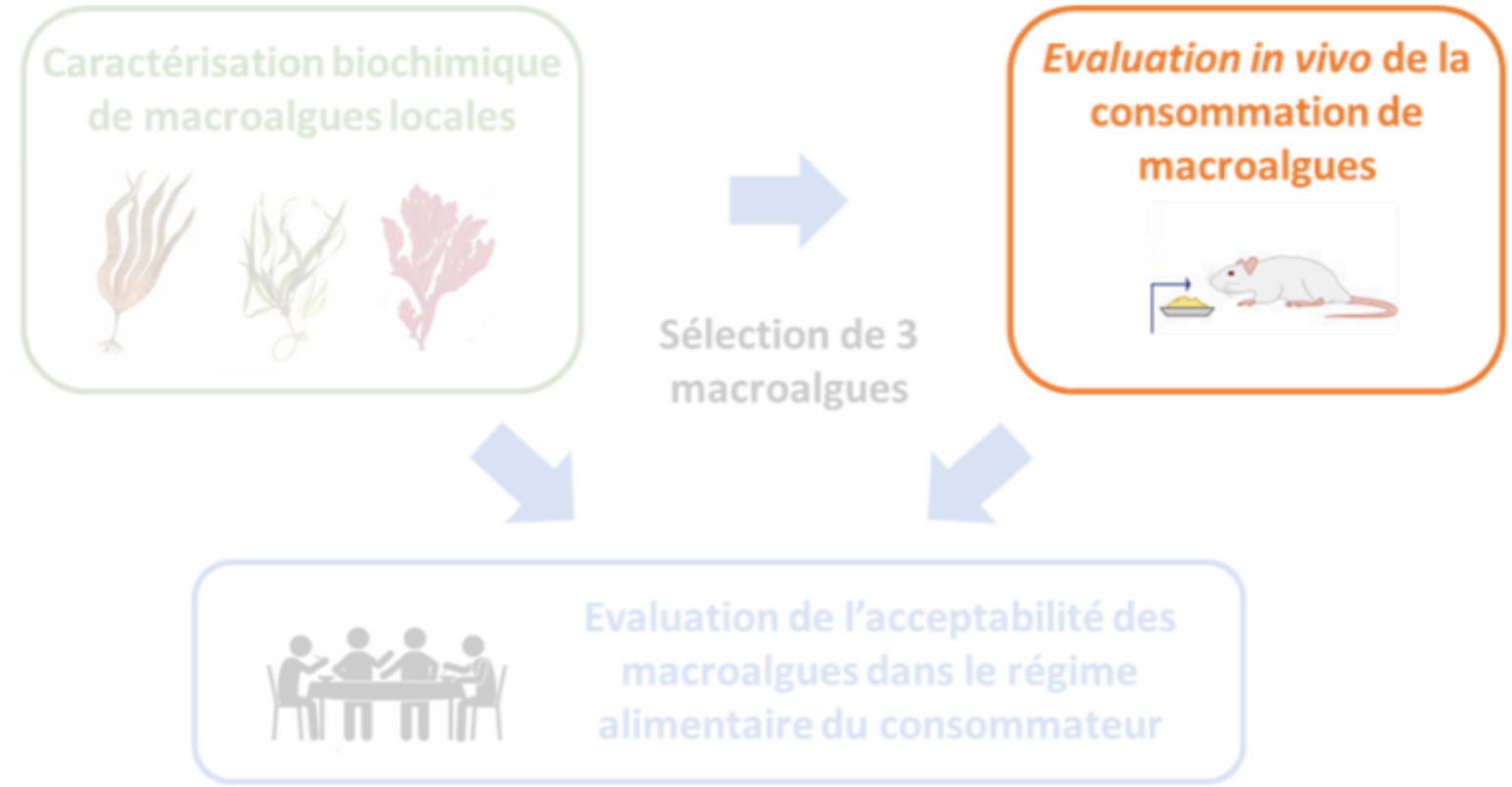
- **Macroalgues entières** peu exploitées comme source alimentaire
  - Nutritionnellement denses et intéressantes
  - Bénéfices santé documentés mais limités

- **Projet ALGOMENU** organisé autour de 3 axes :



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  - Nutritionnellement denses et intéressantes
  - Bénéfices santé documentés mais limités

- **Projet ALGOMENU** organisé autour de 3 axes :



<u>Évaluation *in vivo* de la consommation de macroalgues</u>

Évaluer les **potentiels effets bénéfiques** de la **consommation d'algues** chez des souris nourries avec un régime hyperlipidique

(1) Sur l'écosystème intestinal

(2) Sur les répercussions métaboliques périphériques

Évaluation *in vivo* de la consommation de macroalgues

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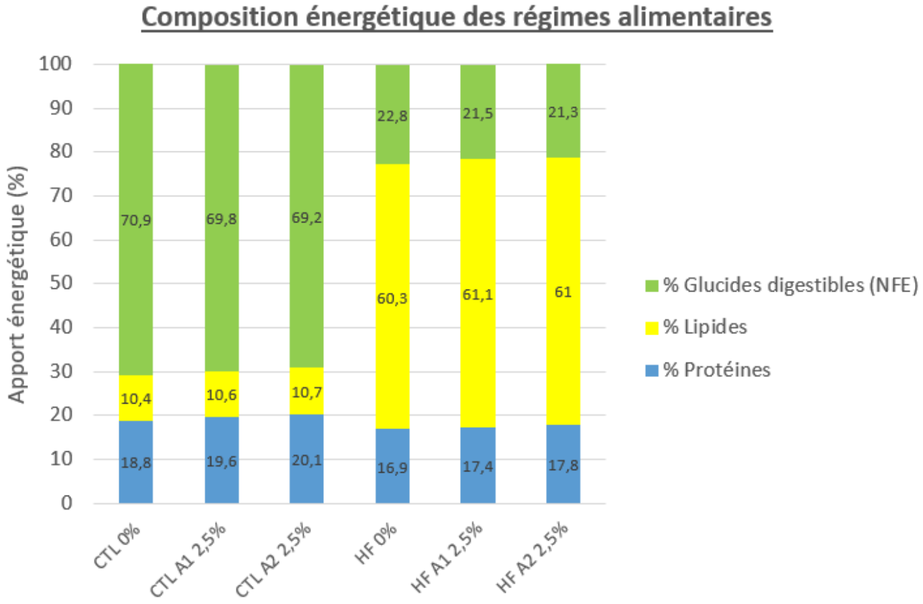
Modèle d'étude :

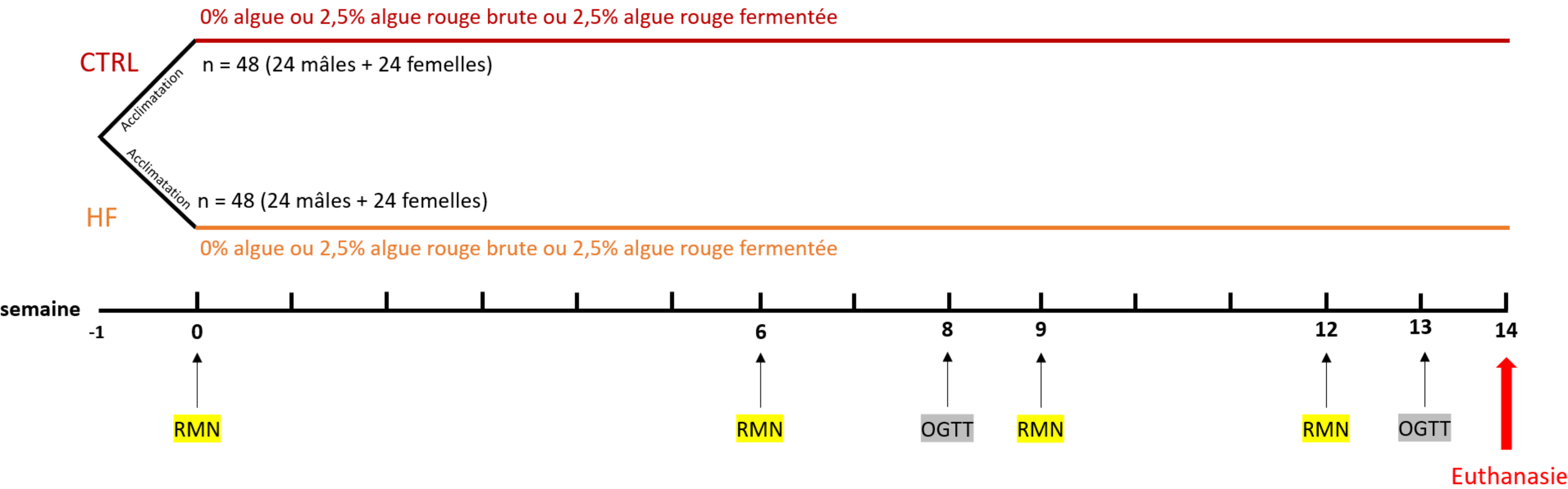


- Souche C57/BL6J
  - 96 souris → 48 mâles et 48 femelles
  - Âgées de 6 semaines à réception
  - Hébergées à l'animalerie Arche sur une période de 14 semaines

Conditions expérimentales :

- 6 groupes de 8 souris / sexe
- Reparties / cage de 4
- 6 régimes
  - CTRL ou HF supplémenté ou non en algue rouge brute ou fermentée (2,5%)





- **0% algue** : n = 16 CTRL (8 mâles + 8 femelles) + n = 16 HF (8 mâles + 8 femelles)
- **2,5% algue rouge brute** : n = 16 CTRL (8 mâles + 8 femelles) + n = 16 HF (8 mâles + 8 femelles)
- **2,5% algue rouge fermentée** : n = 16 CTRL (8 mâles + 8 femelles) + n = 16 HF (8 mâles + 8 femelles)

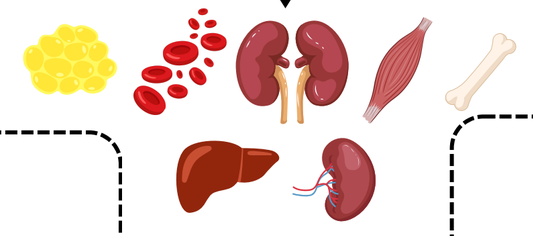


14 semaines de régime obésogène

+/- algue



Euthanasie



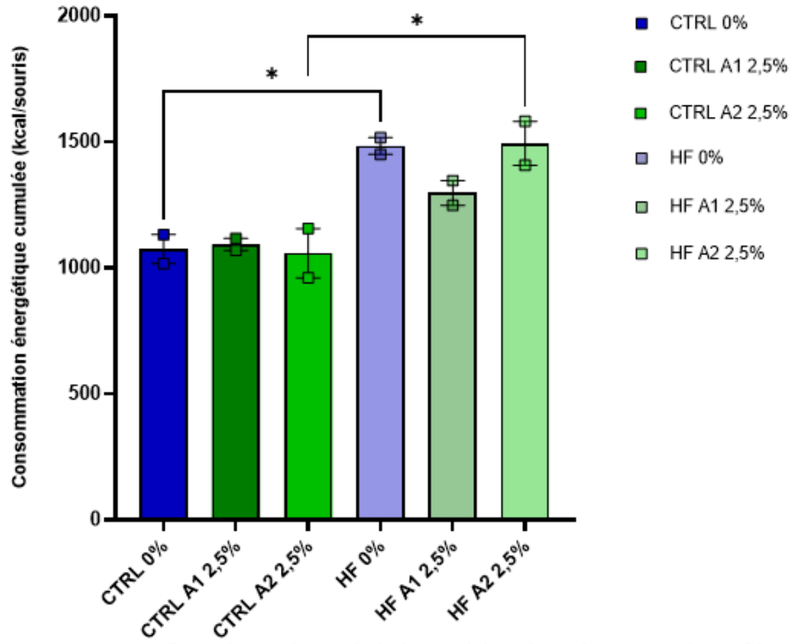
Écosystème intestinal

- Composition du microbiote cæcal
- Métabolome cæcal
- Expression génique et protéique (jéjunum et côlon)
- Analyse histomorphologique (jéjunum et côlon)

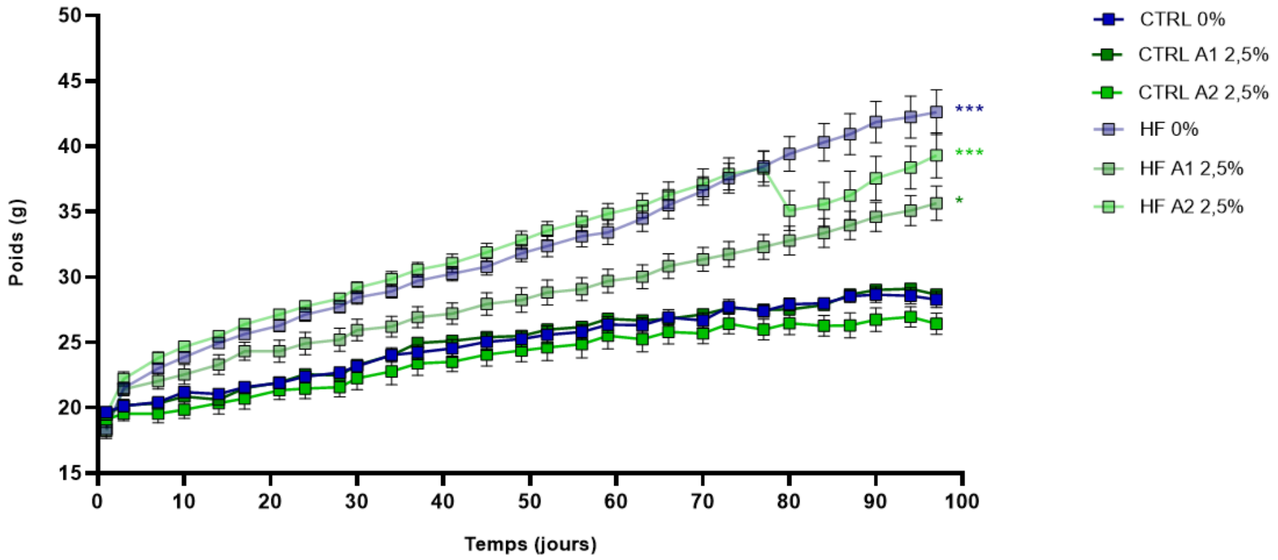
Répercutions métaboliques périphériques

- Prise alimentaire, gain de poids, composition corporelle (MG/MM)
- Métabolismes glucidiques et lipidiques : OGTT, paramètres biochimiques circulants
- Expression génique de marqueurs métaboliques (foie, TA)
- Analyse histomorphologique (foie, reins et rate)
- Métabolisme des métaux (foie, reins, rate, os)

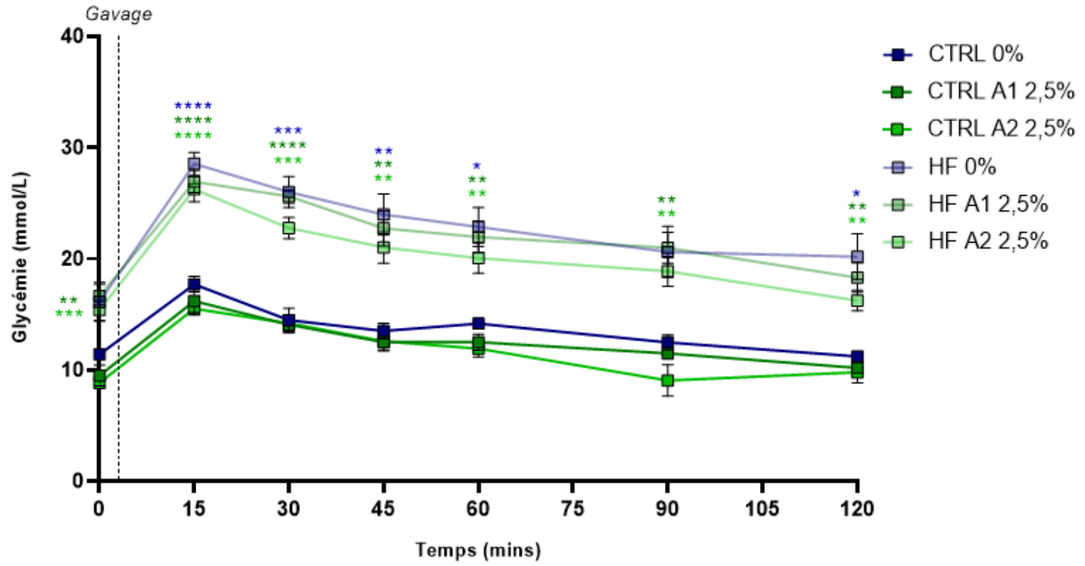
Consommation énergétique cumulée chez les souris mâles



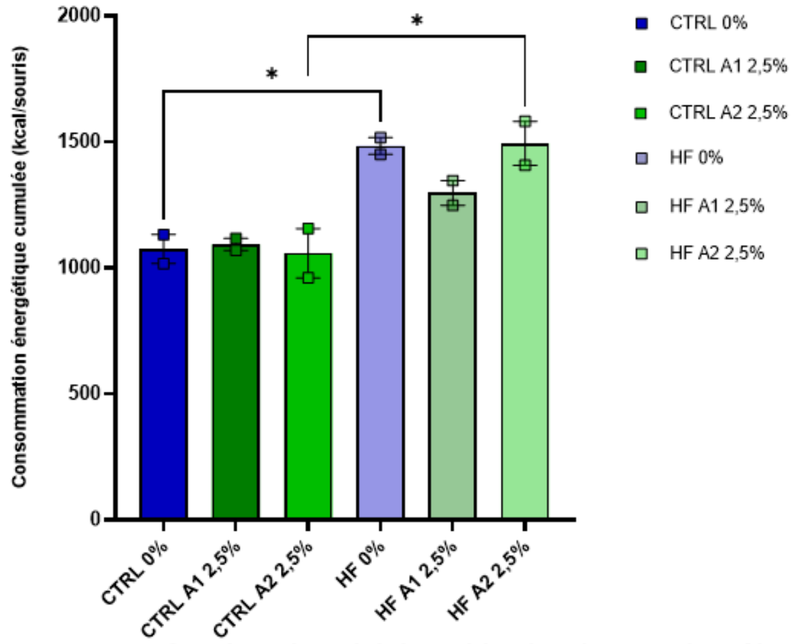
Courbes de suivi du poids chez les souris mâles



Suivi de la glycémie post-gavage au glucose chez les souris mâles (semaine 13)



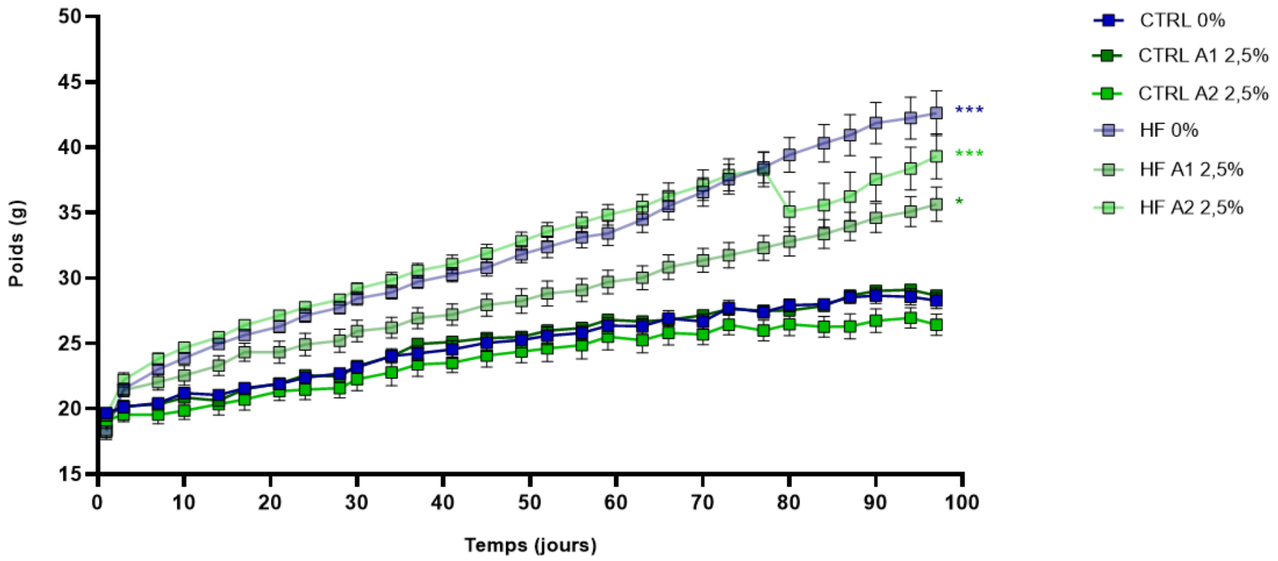
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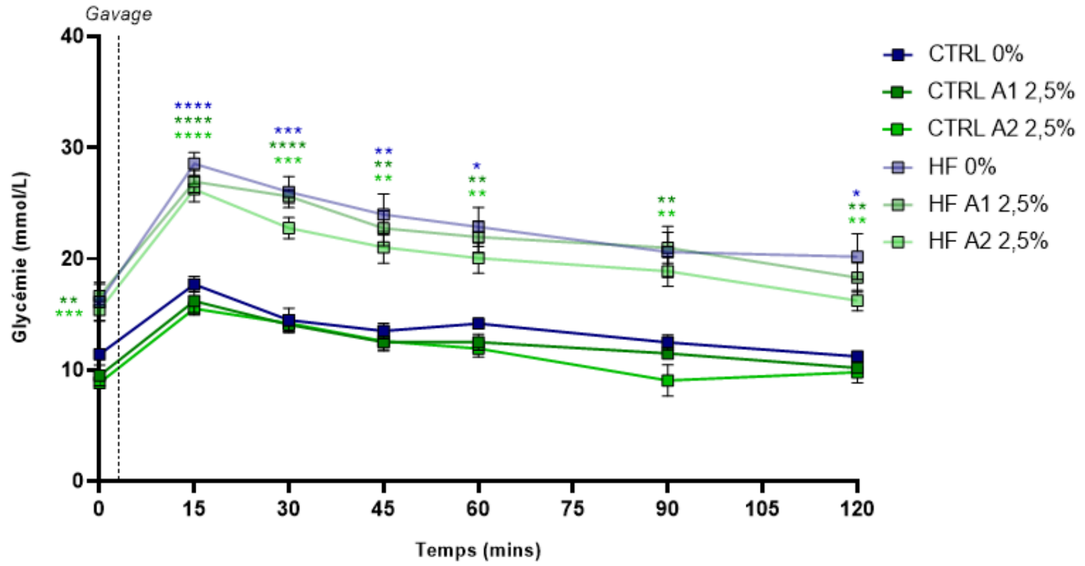
→ **La forme brute de l'algue rouge** semble limiter la **consommation énergétique** et la **prise de poids** sous régime HF chez les **souris mâles**

→ La **réponse au glucose** semble altérée sous régime HF, **indépendamment de la forme de l'algue**

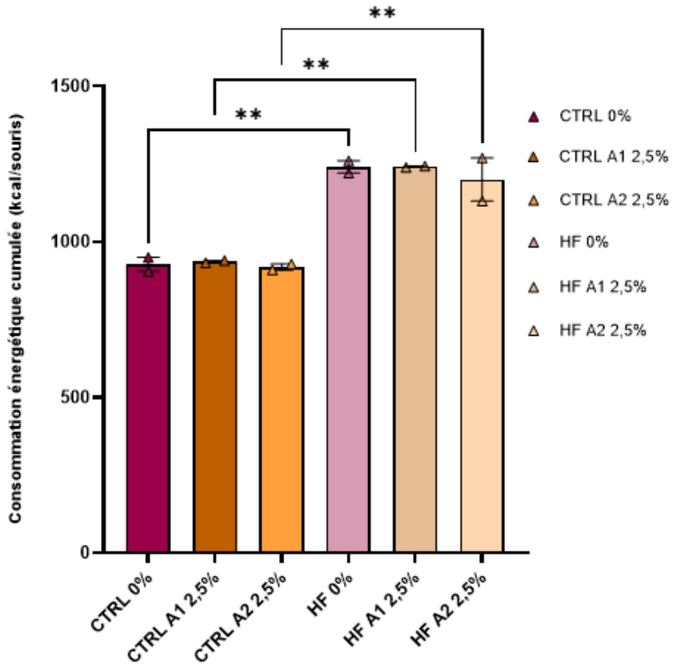
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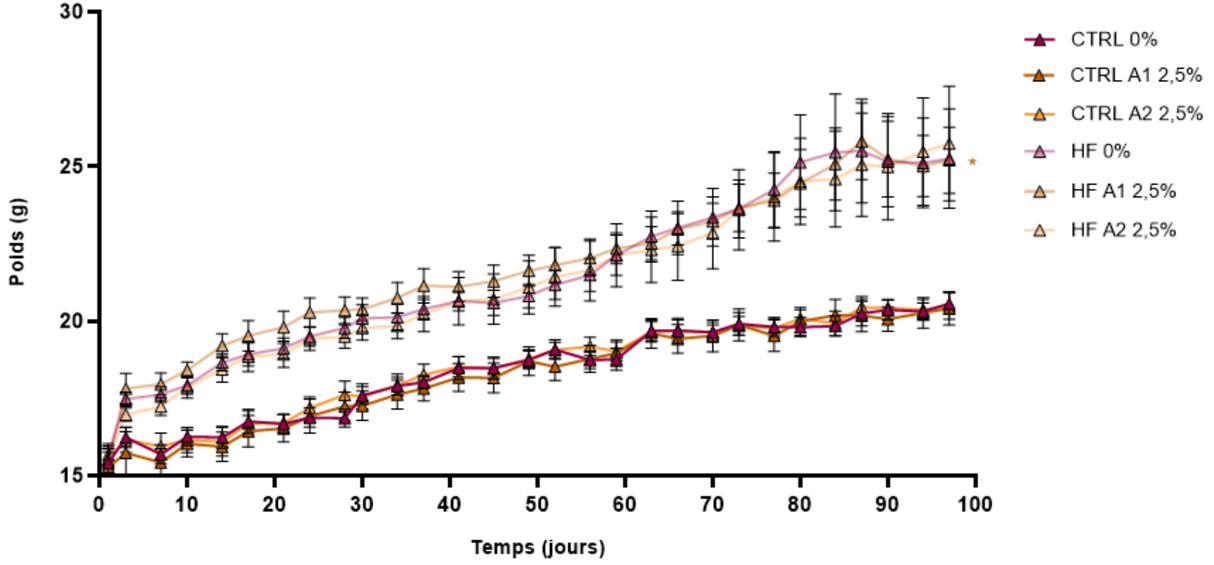
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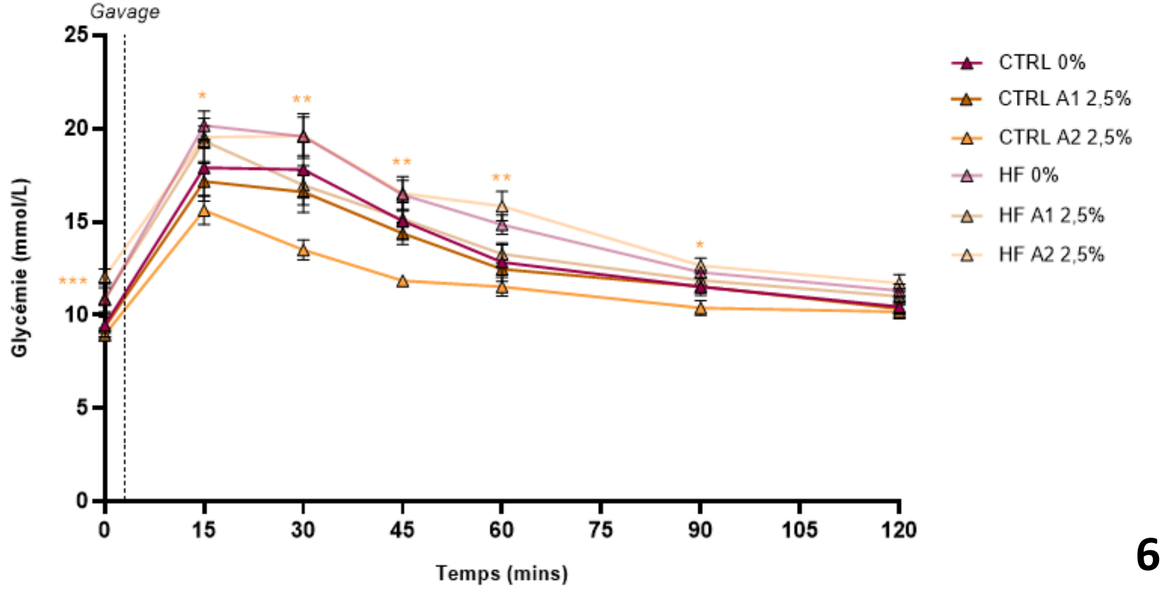
Consommation énergétique cumulée chez les souris femelles



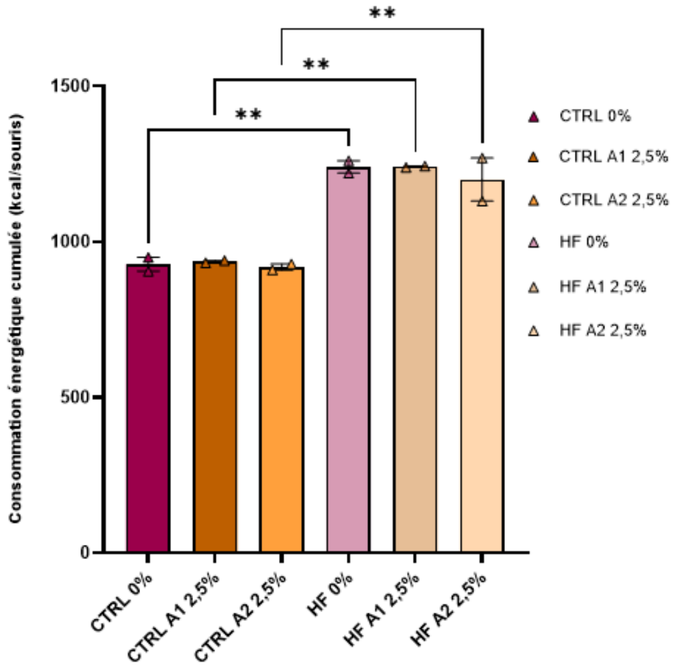
Courbes de suivi du poids chez les souris femelles



Suivi de la glycémie post-gavage au glucose chez les souris femelles (semaine 13)



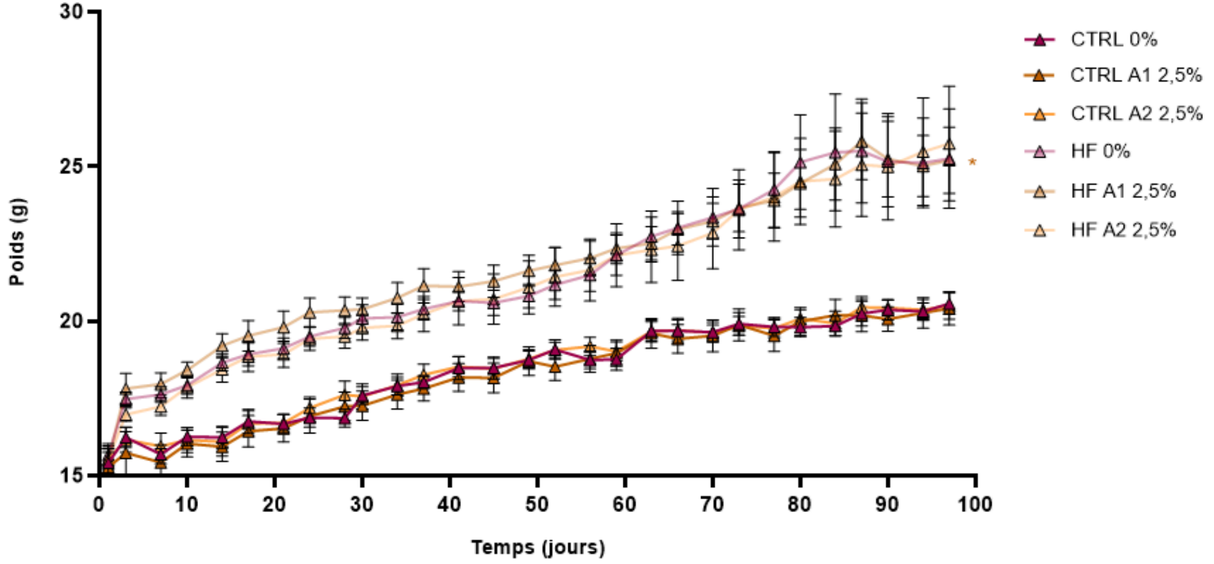
Consommation énergétique cumulée chez les souris femelles



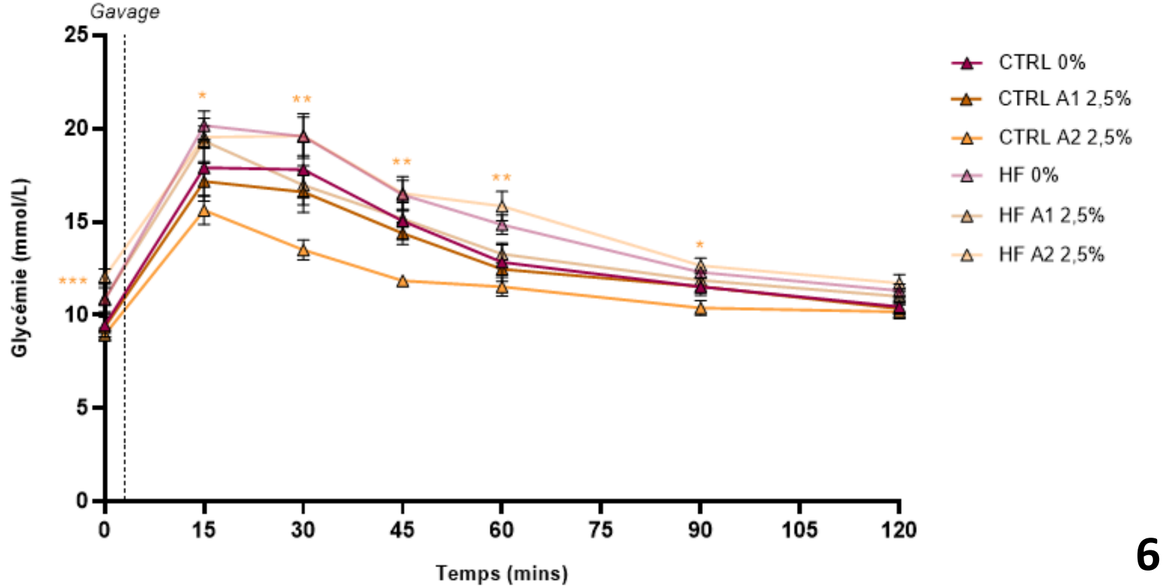
→ **La forme de l'algue rouge** semble peu influencer la **consommation énergétique** et la **prise de poids** induites par le régime HF chez les **souris femelles**

→ La **réponse au glucose** semble altérée sous régime HF supplémenté en **algue rouge fermentée**

Courbes de suivi du poids chez les souris femelles



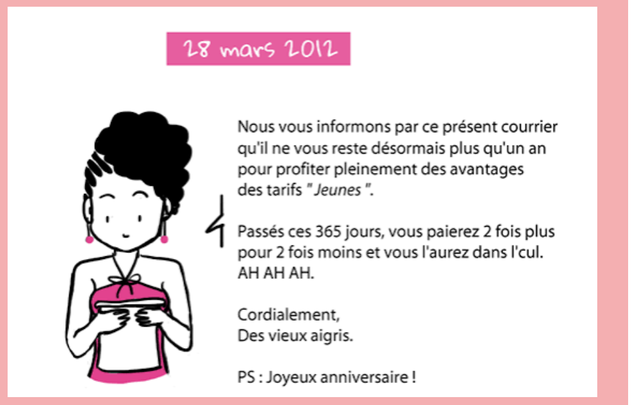
Suivi de la glycémie post-gavage au glucose chez les souris femelles (semaine 13)





HAPPY 25 Elise !

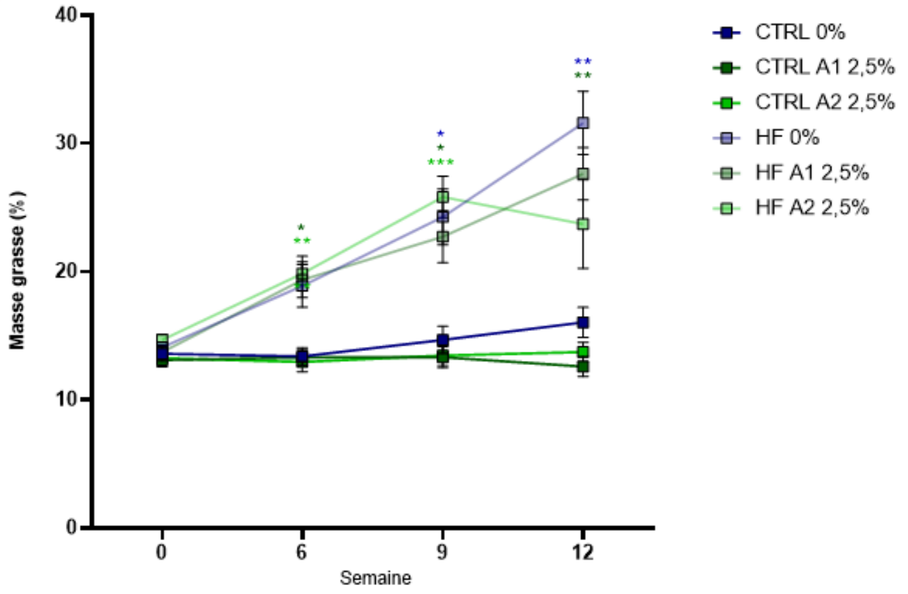




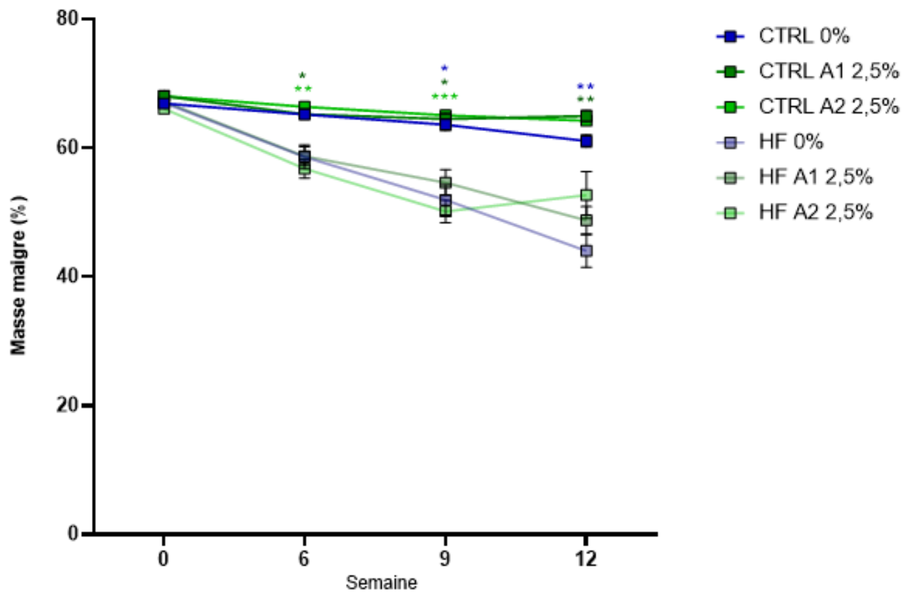
MERCI POUR VOTRE ATTENTION

RMN

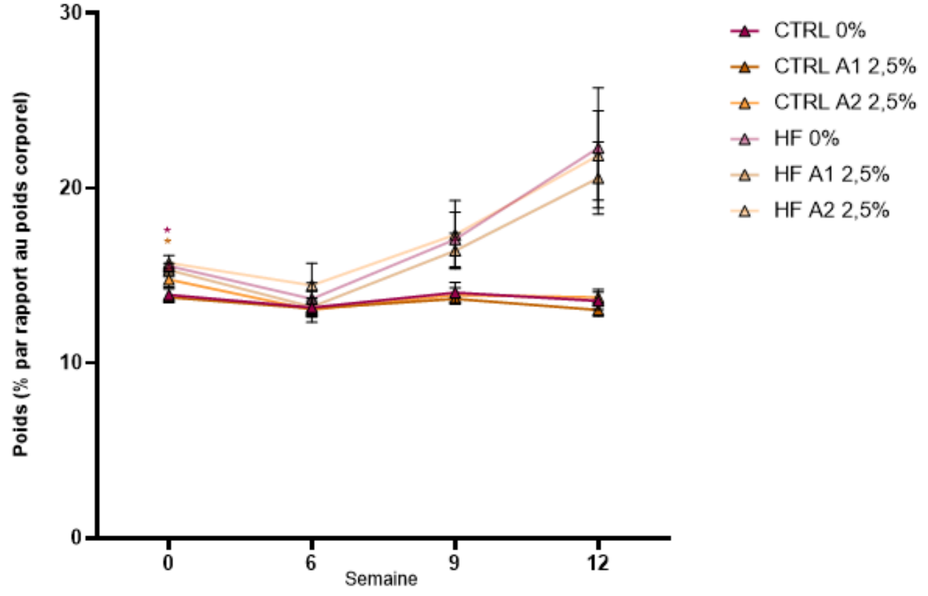
Suivi de la masse grasse par RMN chez les souris mâles



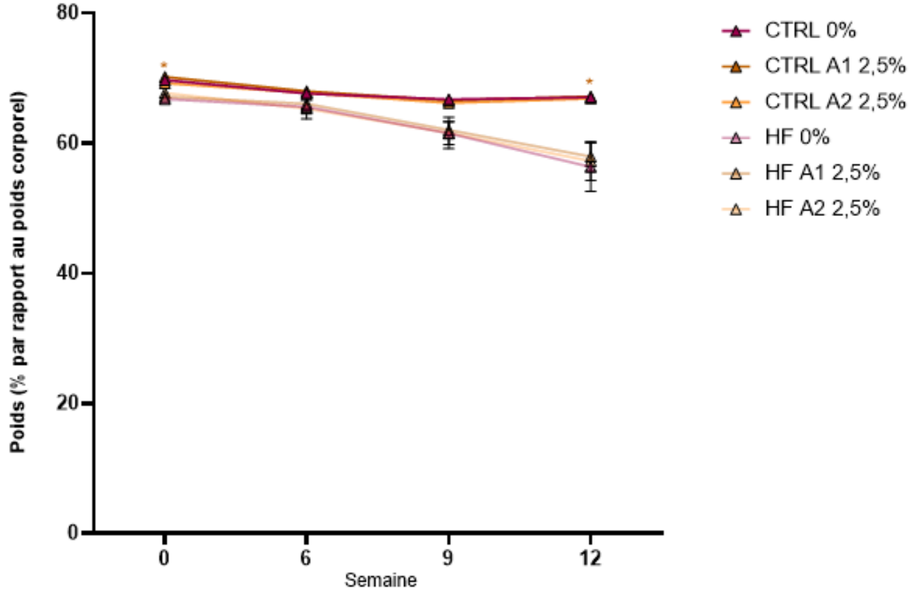
Suivi de la masse maigre par RMN chez les souris mâles



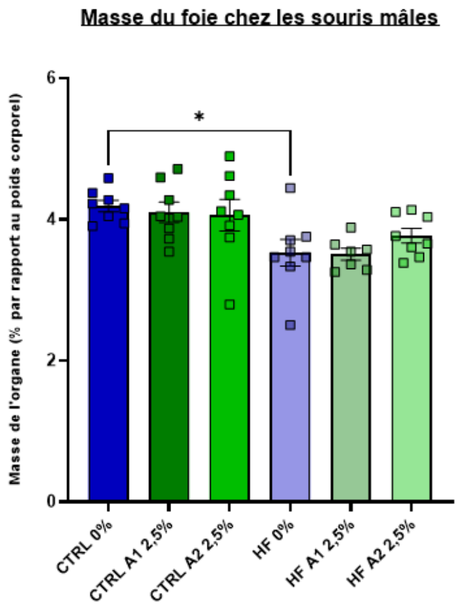
Suivi de la masse grasse par RMN chez les souris femelles

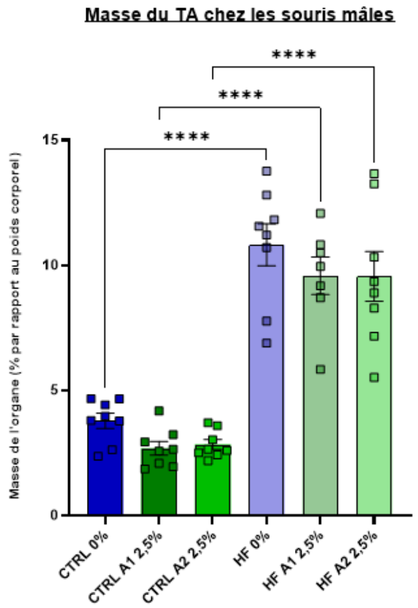


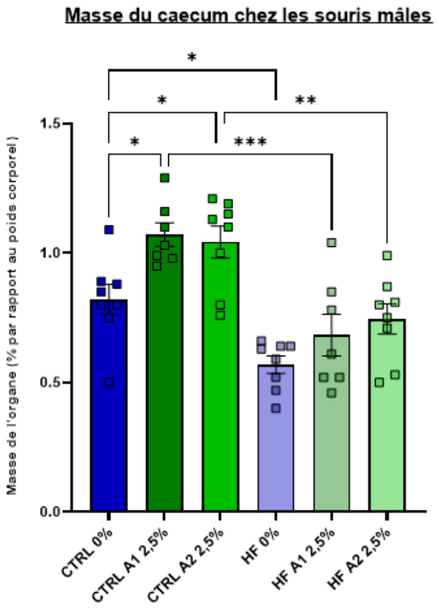
Suivi de la masse maigre par RMN chez les souris femelles

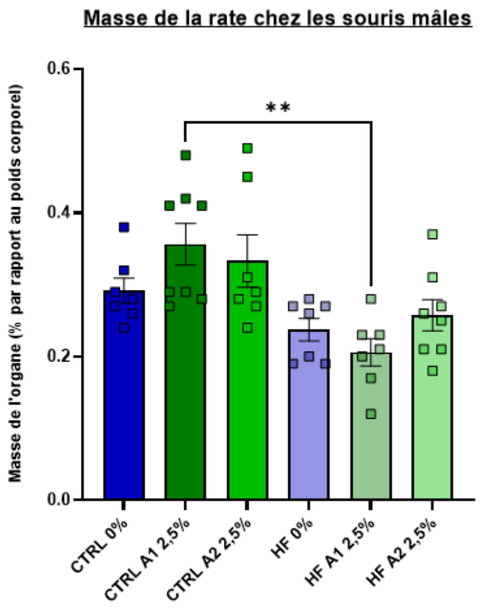


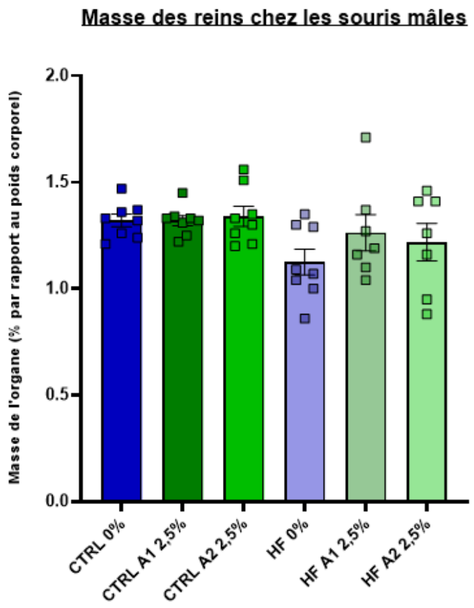
Poids des organes

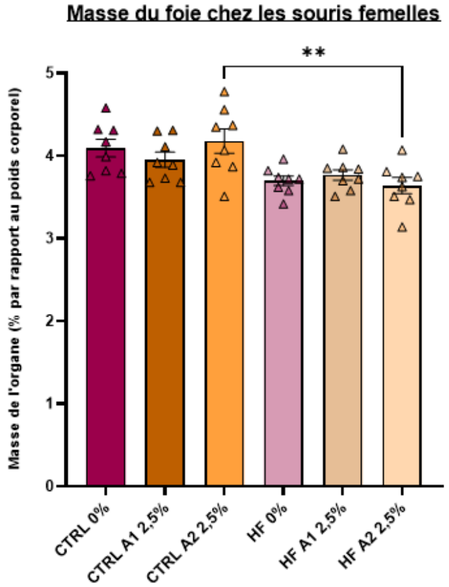


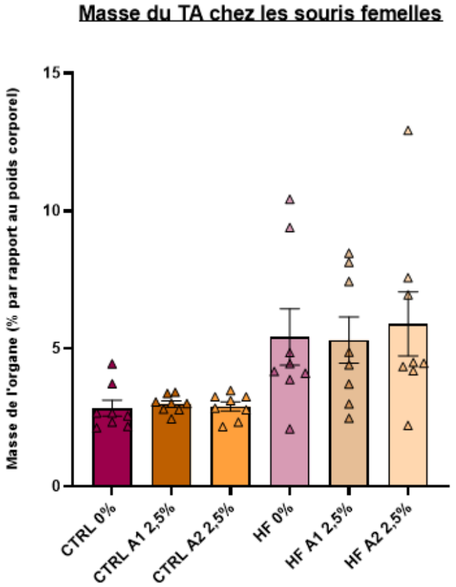


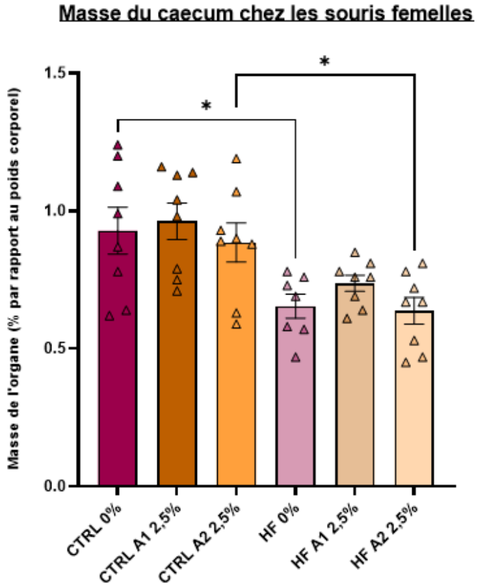


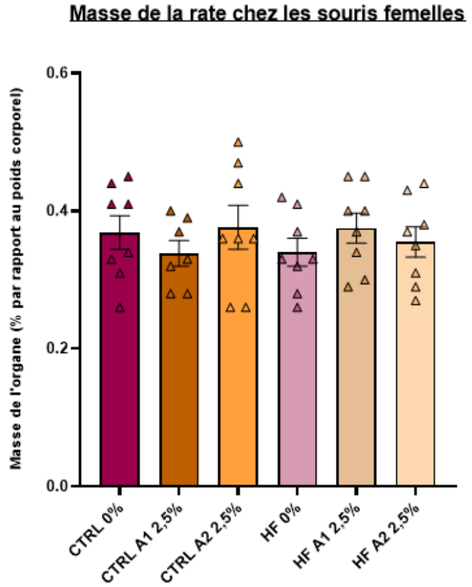


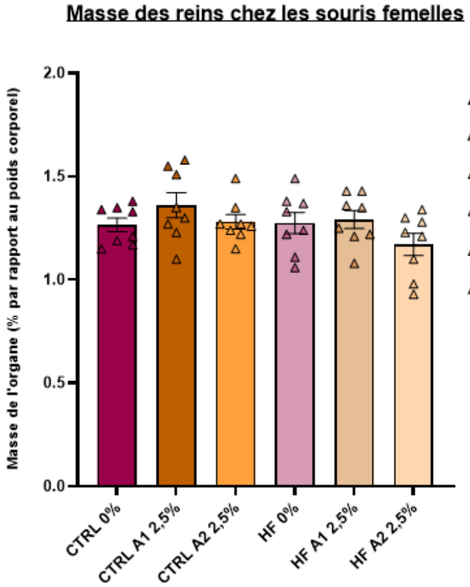












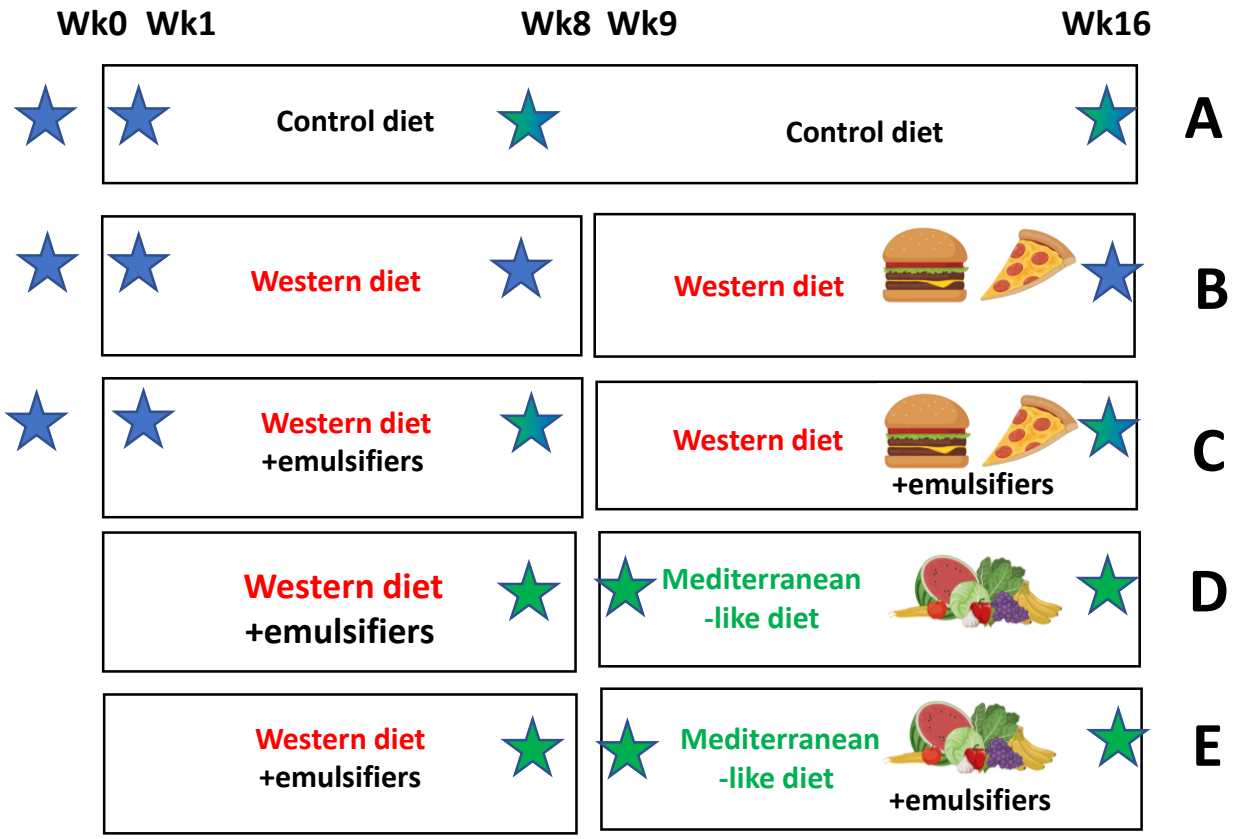
Projet JEMINI

Financement : PEPR-SAMS

Calendrier: novembre 2026 – février 2028

Objectif = évaluer le rôle du microbiote duodéno-jéjunal dans les altérations métaboliques et comportementales lors de la mise en place de l'obésité ou lors d'une perte de poids associée à un régime de type Méditerranéen

Protocole





N = 50 Yucatan female mini-pigs (16 mth of age)

A vs. B vs. C: longitudinal effect of WD or WD+emulsifiers (3 timepoints: 1, 8 & 16 wks)
C vs D vs E: impact of dietary switch from WD + emulsifier to Med-like diet w/ or wo/ emulsifiers (2 time points, 9 & 16wks)

Régimes

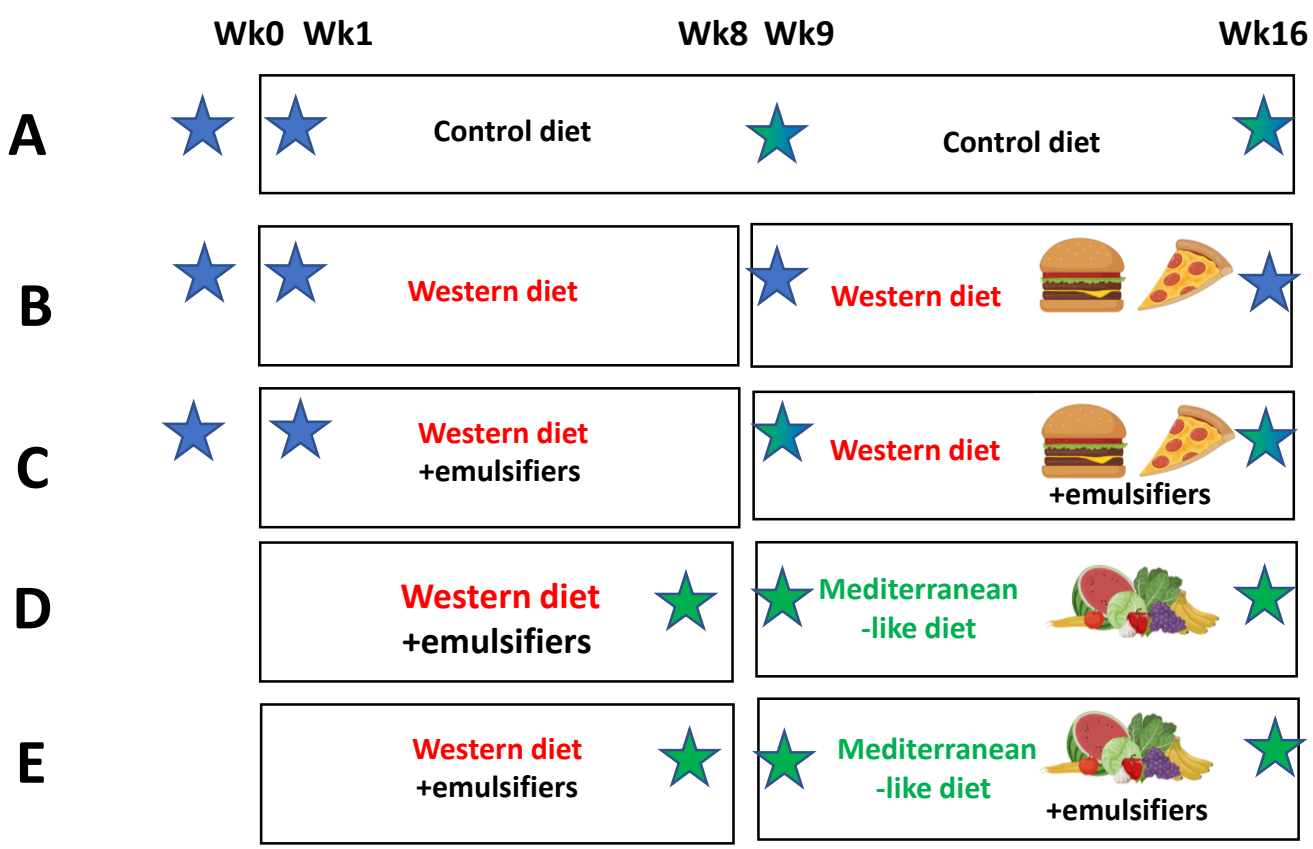
	Mini-Pig standard	Western Diet, historique	Western Diet, nouvelle proposition	Mediterranean Diet
Composition				
Blé tendre	10.00	6.50	15.30	19.36
Maïs				24.92
Orge	31.45	12.00		14.63
Coques de soja	12.20	8.00		
Tourteau de tournesol non décortiqué	10.00	8.00		
Tourteau de soja 48	7.44	12.00	29.60	
Saccharose		20.00	20.00	
Amidon de maïs		6.50	17.13	
Saindoux		10.00	11.35	
Féverole à fleurs colorées				2.99
Graine de lin				3.00
Lupin blanc				2.98
Concentré de protéines solubles de po				5.49
Son de blé tendre	25.00	14.00		7.01
Poudre de courgette				5.00
Poudre de poivron rouge				2.00
Poudre de tomate standard				5.00
Poudre de noix				2.00
Herbes de provence				0.50
Mélasse de canne	1.00		1.00	1.00
Sel	0.57	0.60	1.88	0.42
Carbonate de calcium	1.29	1.30	2.36	2.45
Phosphate monocalcique Cooperl	0.55		0.89	0.76
Phosphate bicalcique		0.60		
Prémix truie	0.50	0.50	0.50	0.50
Total	100	100	100	100
Caractéristiques				
MAT, %	15.0	12.3	15.0	15.0
Matière Grasse, %	2.2	11.4	12.2	4.8
TDF (d'après Le Gall JRP 2011), %	38.4	25.7	15.9	20.8
Sucres, %	4.4	22.8	23.3	6.1
AGS, %MG	14	37	39	12
C18:2/C18:3	10	10	10	2
Sodium, %	0.24	0.24	0.75	0.25
EB, MJ/kg	15.99	18.31	18.11	15.66

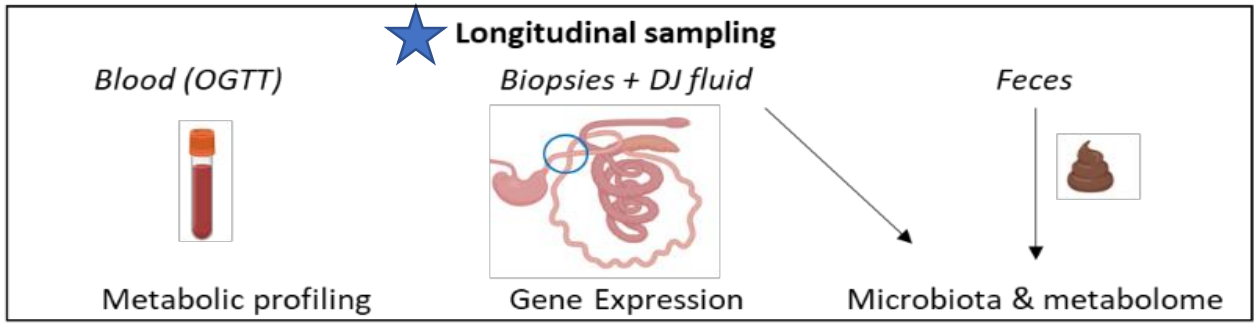
Emulsifiants / épaissisants

mélange final pour 1T d'aliment	(mg)
Lecithin (E322)	2,4
Amidons modifiés (E1450,E1420,E1404)	45,9
Gomme xanthane (E415)	35,4
Pectine (E440)	12,1
Di et monoacyl d'acides gras (E471)	12,2
Carraghenanes (E407)	1,4
Sodium carbonate (E500)	128,3
Gomme guar (E412)	22,5
Diphosphate (E450)	19,3

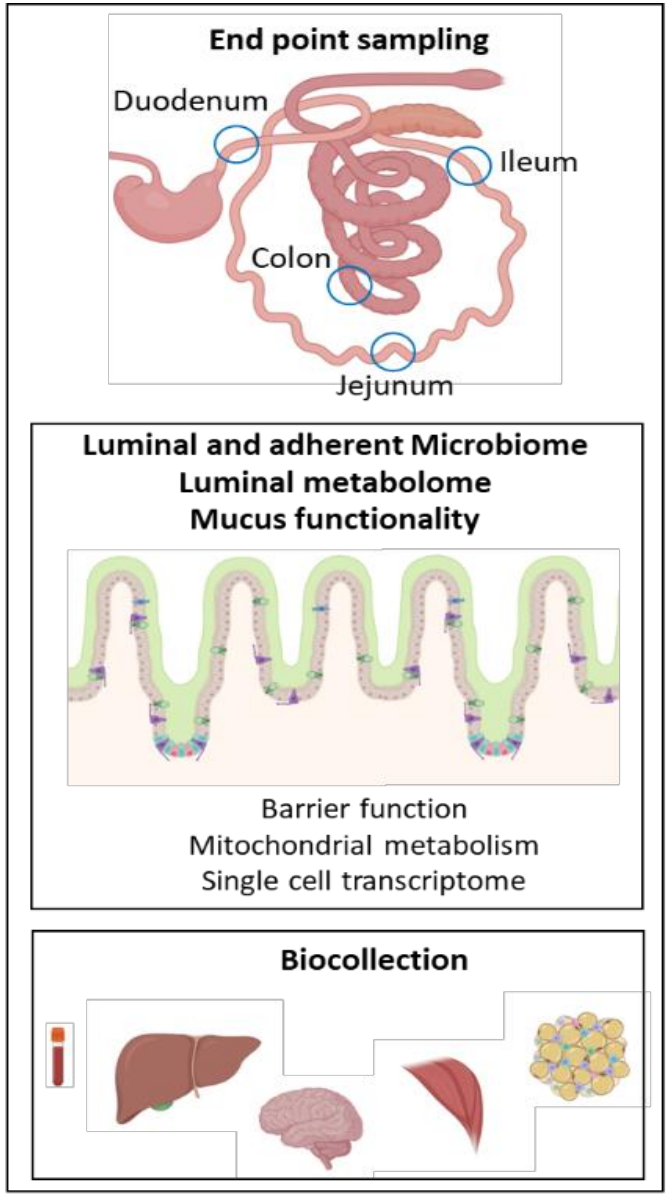
Basé sur la consommation moyenne des français (étude Nutrinet Santé, Chazelas et al., 2021 Sci Rep)

Prélèvements





+ eating behavior







PHOENIX : nanomédecine pour la transplantation d'organes

https://vimeo.com/1072128797
mdp: spleen

Alexandre Chebaro, Karim Boudjema – CHU Rennes
David Val-Laillet – INRAE

Funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.

Présentation du projet

L'immunosuppression au long cours chez les greffés d'organe solide cause des complications aigües et/ou chroniques pouvant amener à la perte du greffon voire au décès du patient sans rejet de l'organe.

Nanoparticules : candidat médicament

- permet d'activer et d'expandre certaines sous-populations lymphocytaires
- cible modulable en fonction du peptide et de l'antigène choisi
- applications : maladies auto-immunes et auto-inflammatoires (diabète, polyarthrite), rejet

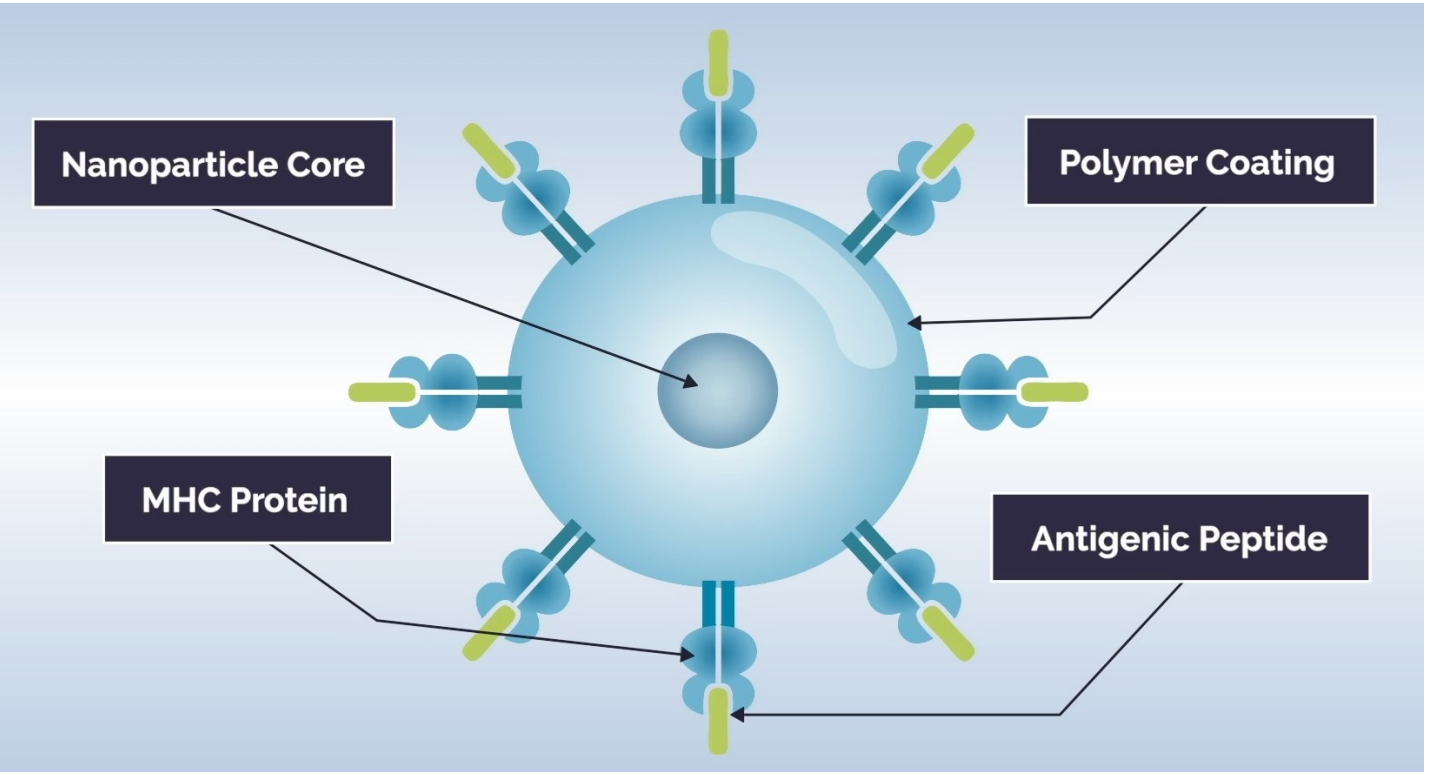
Le projet PHOENIX est piloté par un consortium et dure 3 ans (04/23 → 04/26)

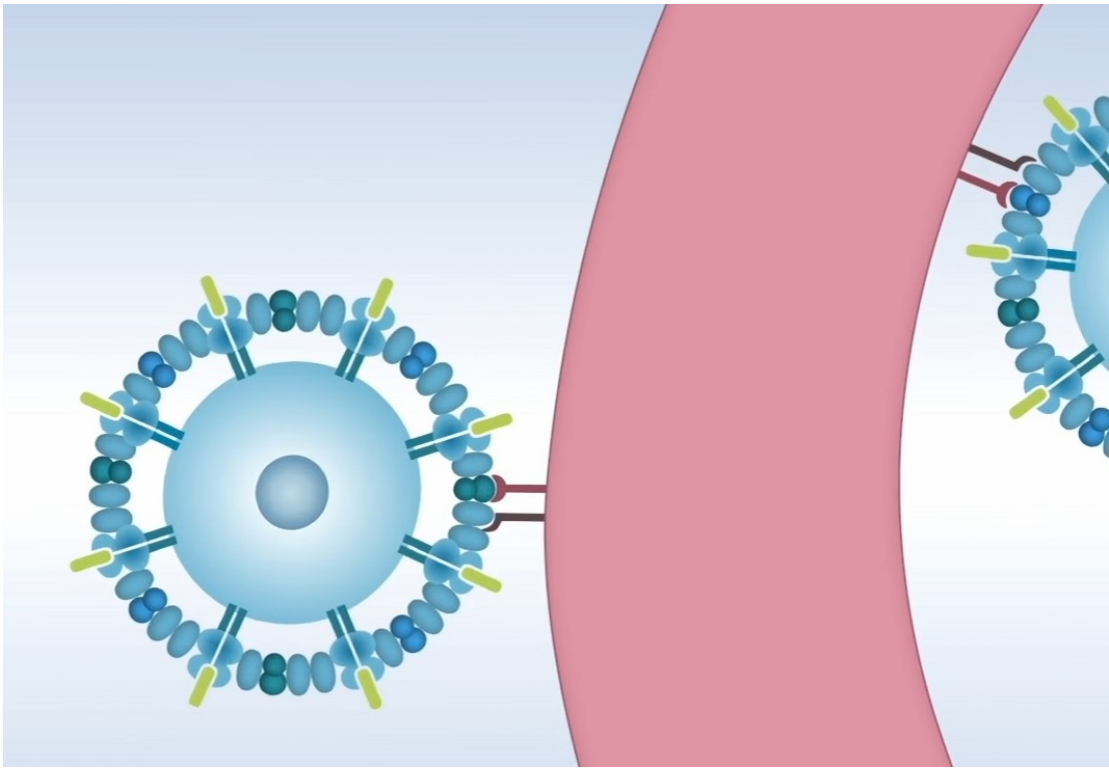
- IDIBAPS (Barcelone, P Santamaria) : production des nanoparticules
- IRFMN (Bergame, G Remuzzi) : transplantation rénale et hépatique (modèle murin)
- INRAE/CHU Rennes (DVL, AC, KB) : transplantation hépatique (modèle porcin)
- Pintail Ltd (Irlande) : management du projet

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Composition des nanoparticules





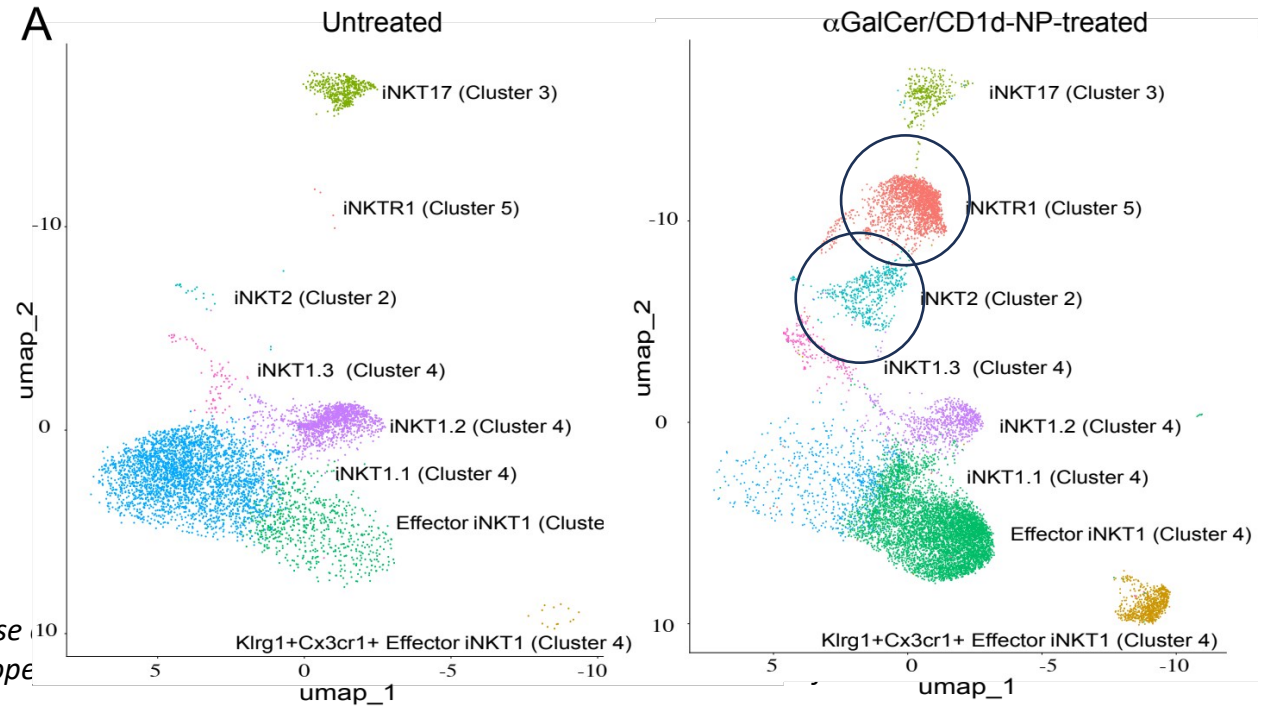
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WP3: Liver transplantation in pigs

Nanoparticules : αGalCer/CD1d

- αGalCer est un glycolipide capable d'activer les LT NK invariants (iNKT) lorsque présenté
- cible dans notre cas : lymphocytes T NK invariants intra-hépatiques
- effet escompté : trans-différentiation des lymphocytes activées en "T reg 1-like", inhibition des mécanismes du rejet aigü cellulaire



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Modèle animal :

- porc en croissance
- 2 à 3 mois
- 20 à 40 kg

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WP3: Liver transplantation in pigs

Deux objectifs :

- T3.1: To observe the therapeutic effects of αGalCer/CD1d-NPs
- T3.2: To observe the pharmacodynamics effects (formation of iNKTR1 cells) in vivo

Hypothèse :

- Treated rejet 67% n = 12
- Control rejet 100% n = 12

Two groups:

- Treated n = 10, 10 doses, 3 weeks treatment course[1]
- Control n = 10, no immunosuppression

Follow-up: 90 days

[1] 12 mg protein-equivalent per dose; POD 1, 3, 5, 7, 9, 11, 13, 15, 17, 19

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Pig donors
(N=20)

Static cold
storage

Pig
recipients
(N=20)

Liver
transplantation

(N=10)

(N=10

empty CD1d-NPs
3/week for 3 weeks

αGalCer/CD1d-NPs
3/week for 3 weeks

follow-up
for 90 days

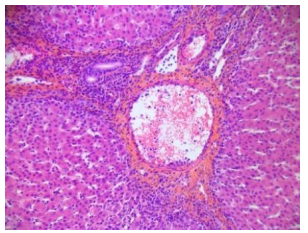
Demonstrate tolerance induced by αGalCer/CD1d-NPs

Main outcome measure: 90-day survival

Graft function



Banff & Suzuki score



FCXM

PHOENIX Study 4
Experiment 1
Task 3.1

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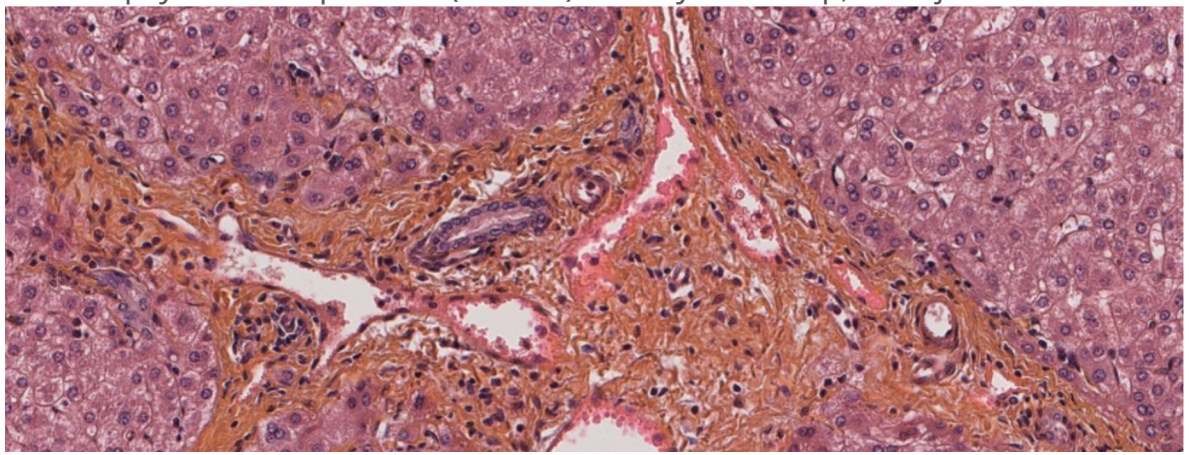
WP3 Main result

The control group did not develop any significant rejection

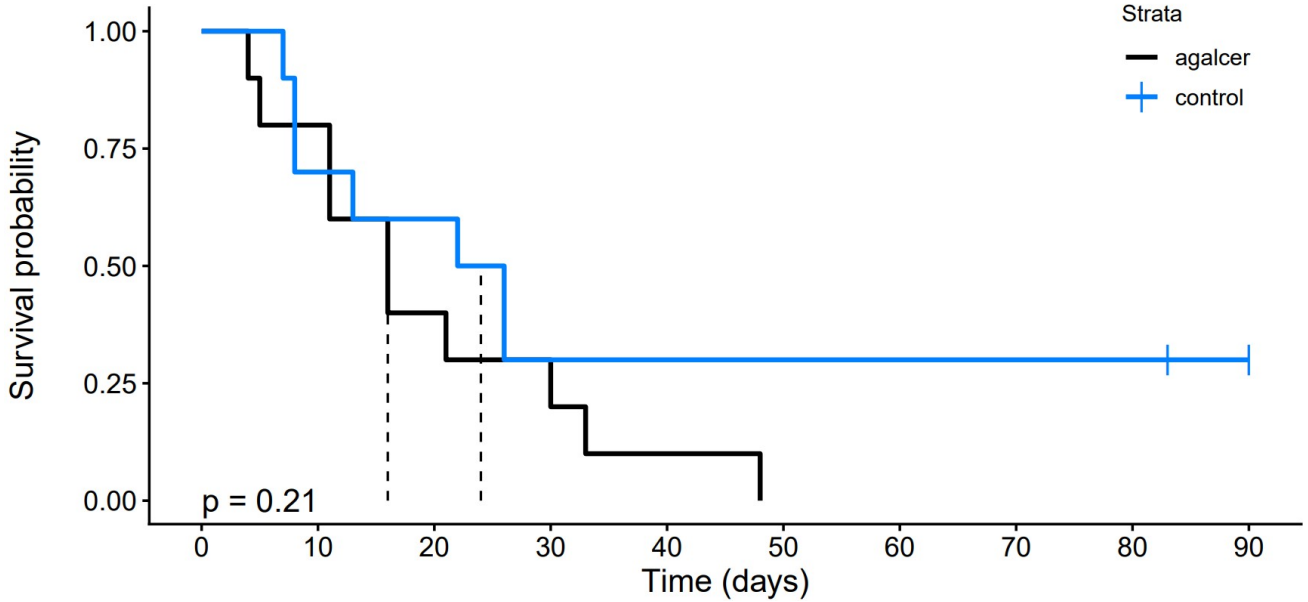
Therapeutic effects of αGalCer/CD1d-NPs could not be assessed in this model

A refined model using donor skin grafts to pre-sensitize recipients is ongoing

Post-mortem biopsy from recipient 10 (control): 90-day follow-up; no rejection



Recipient survival after liver transplantation (treated vs. control group)



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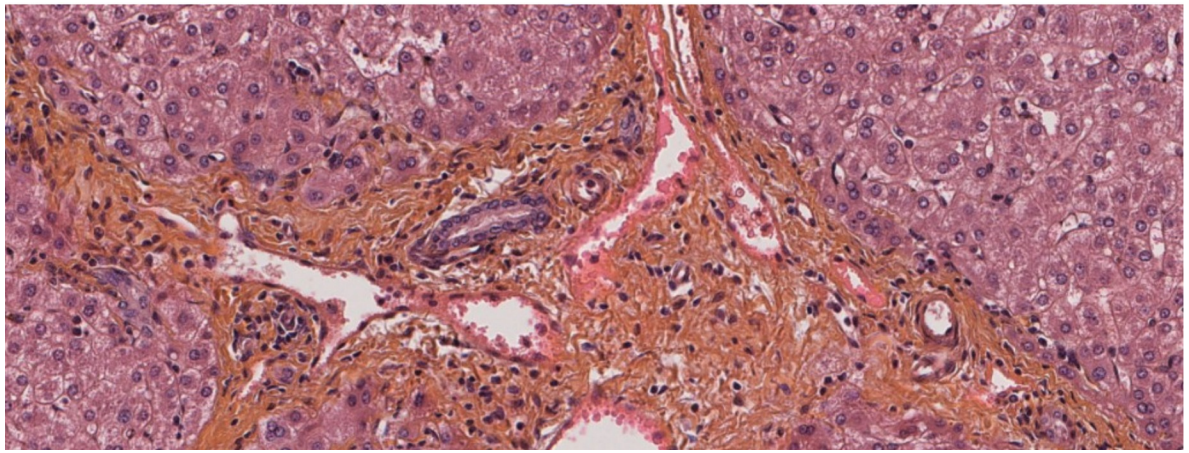
Histological results and model limitation

The was no difference between groups in terms of acute rejection.

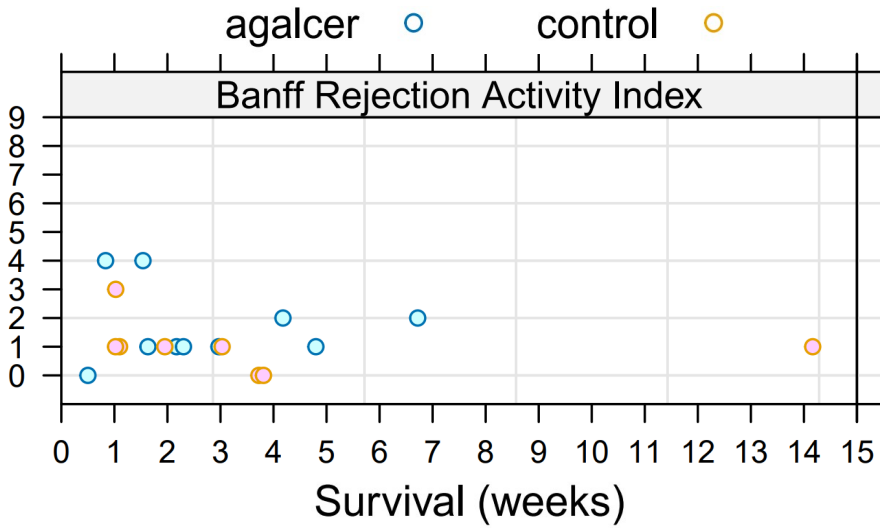
No clinically significant acute rejection in the control group.

The non-sensitized model is insufficient to evaluate the effect of NPs on rejection.

Post-mortem biopsy from recipient 10 (control): 90-day follow-up; no rejection



Banff score according to recipient survival



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Recipient follow-up and survival

20 planned transplants were completed
2 animals still undergoing follow-up at the end of RP2

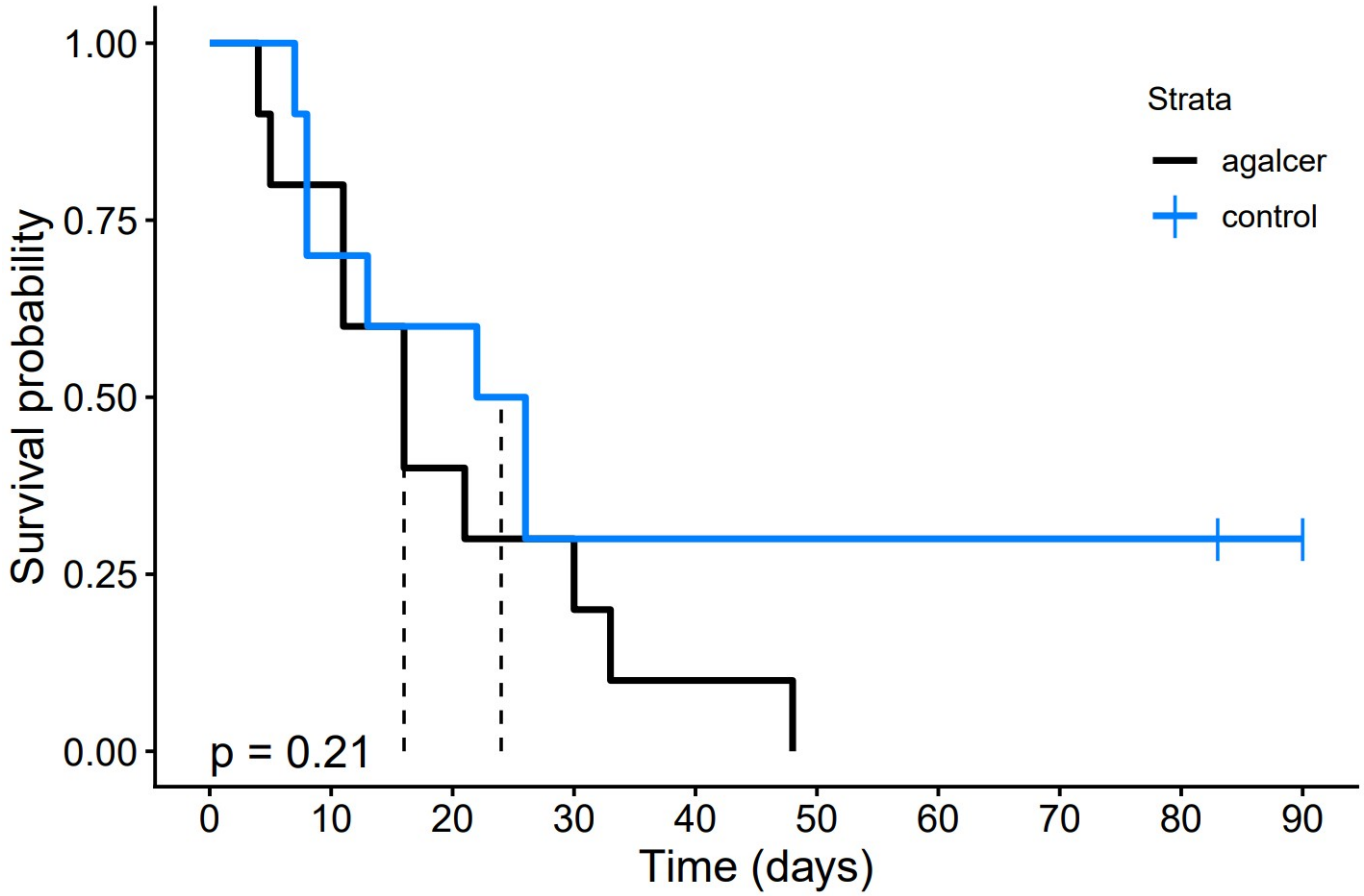
Survival was equivalent in both groups

Causes of experiment termination at the end of RP2:

- medical complications 30%
- surgical complications 30%
- unknown complication 20%
- follow-up complete 15%

Main contributors included catheter or intra-abdominal infections, gastric ulcers with hemorrhage or perforation, adhesions and/or small bowel volvulus, and bile duct leakage in a minority of cases.

Recipient survival after liver transplantation (treated vs. control group)



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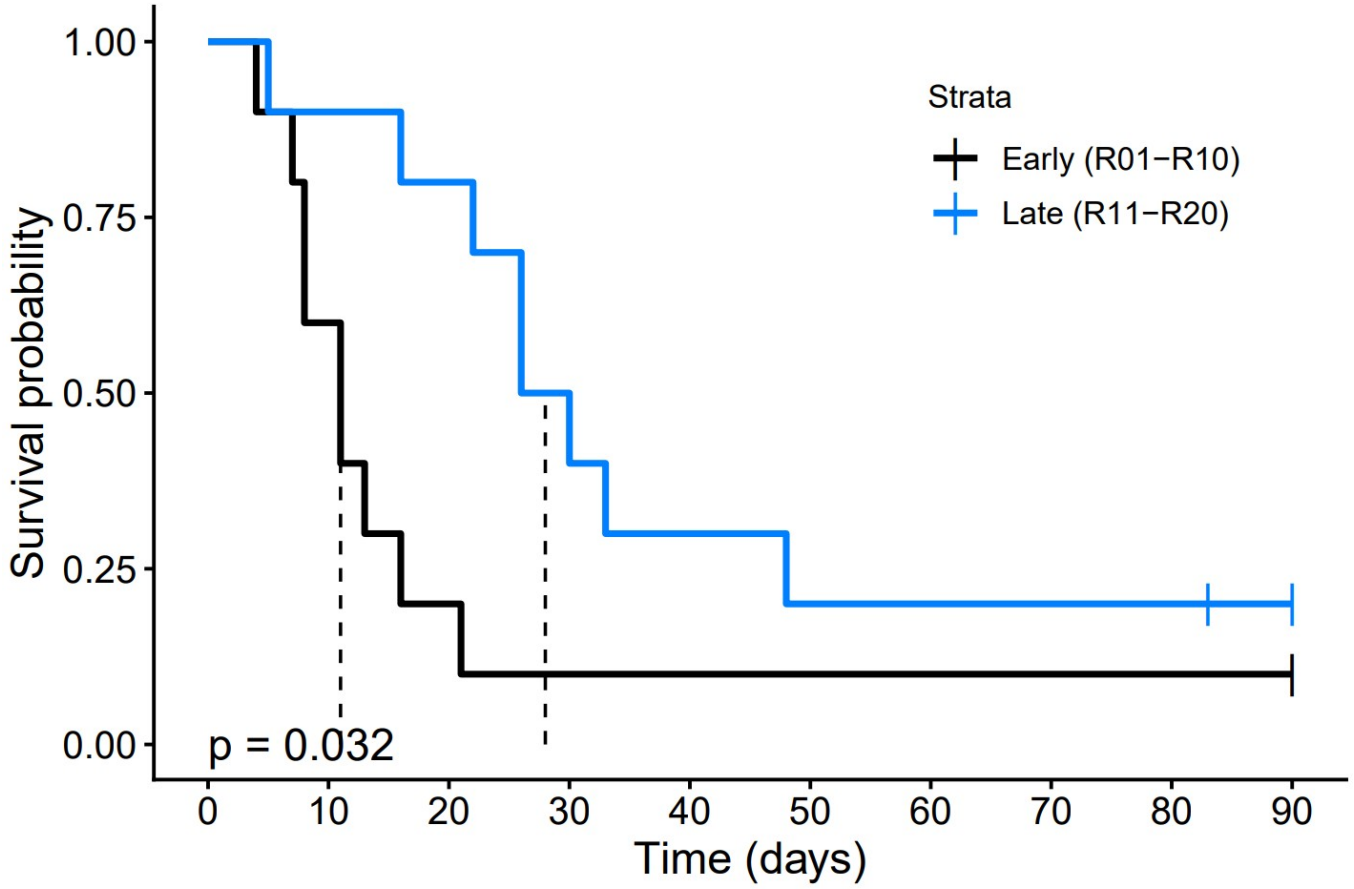
Learning-curve effect

Survival was longer in the late period (R11-R20) than in the early period (R01-R10).

This learning-curve effect is likely due to the changes we made in peri-operative management over time.

Median survival:	18.5 days [11, 33]
Early cohort:	11 days [8, NE]
Late cohort:	28 days [22, NE]
Log-rank	p = 0.0322

Recipient survival after liver transplantation (early vs. late period)



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Pre-sensitized model

Non-sensitized recipients did not reliably reject liver grafts.

As reliable pig rejector strains do not exist, a proposal of a new model with pre-sensitized recipients was accepted by the consortium in December 2025 :

- Skin grafting from the future liver donor two weeks before liver transplant
- Liver transplant procedure and follow-up identical to the non-sensitized model

Start of experiments: September 2026

n = 12 (6 in each group)

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T3.1 and T3.2 experiments during RP2

T3.1 experiments

- 20 liver transplant experiments performed, 10 in each group
- First transplant: March 4th 2025 – Last transplant: March 24th 2026
- At the end of RP2, two experiments were still undergoing follow-up

T3.2 experiments

Lymphocyte isolation performed on 14 liver samples during RP2:

- 7 “dry runs” on native organs to establish a baseline population
- 5 from control animals
- 2 from treated animals

Frozen samples were sent to FCRB/IDIBAPS for staining and analysis.

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Model refinements

We addressed several post-operative complications by refining the model with each iteration.

Infections

- Symptoms: fever, listlessness, anorexia, reaction to injections

Introduction of antibiotic course (amoxicillin) during the first week of follow-up
Previously: single dose on the day of transplantation

Gastric ulcers

- Symptoms: fever, listlessness, anorexia, hematemesis/dark feces

Intravenous full-dose pantoprazole once daily until POD 21, on-demand thereafter
Previously: oral low-dose lansoprazole once daily until POD 7

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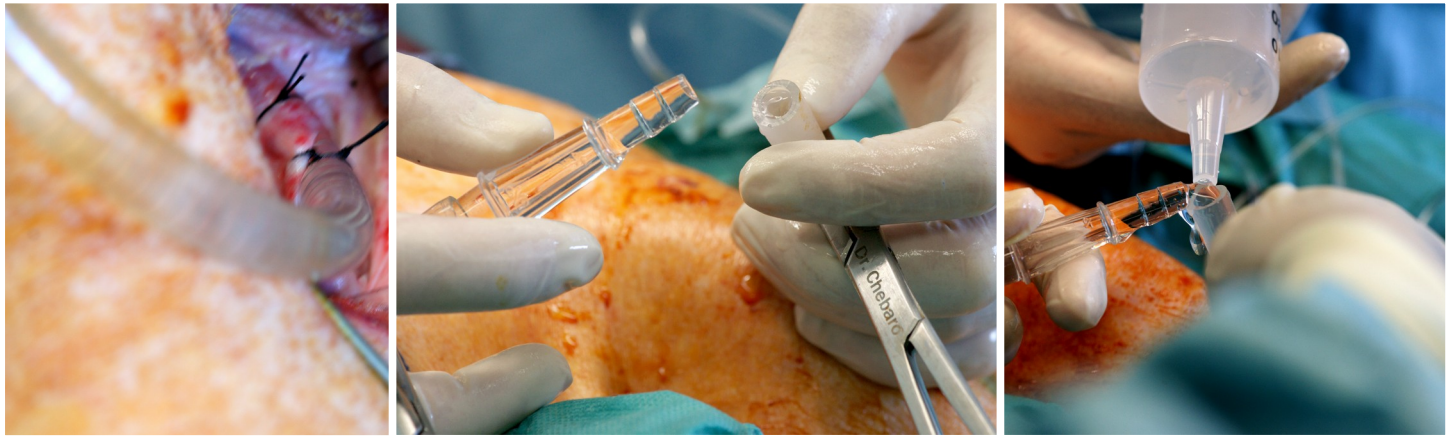
T3.1 surgical procedure

All procedures were performed by the same operator using the same technique

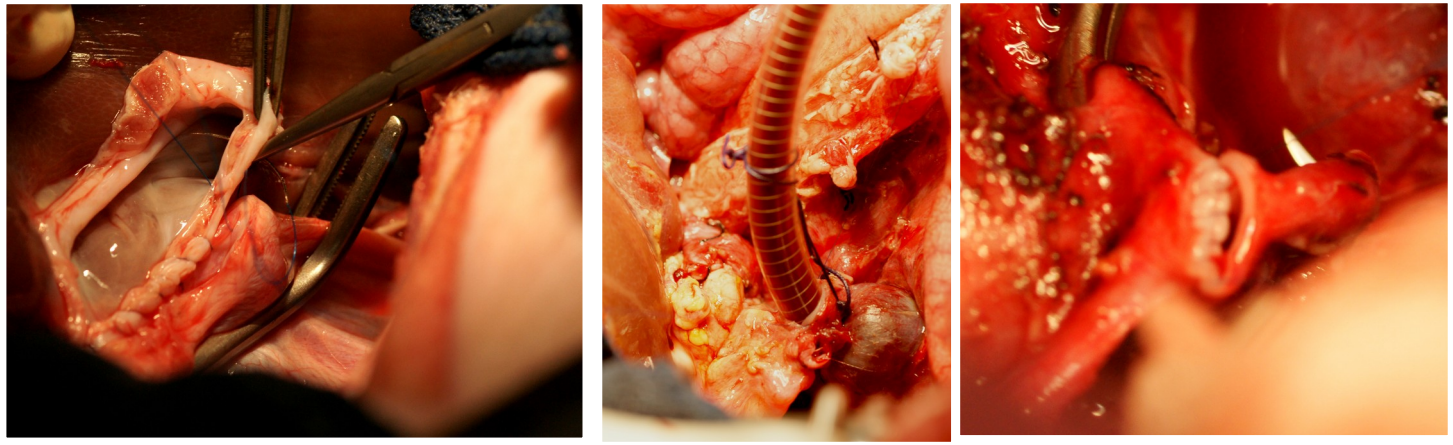
No adverse event during surgeries

Key figures:

- Recipient operation: 3 hours
- Cold ischemia: < 3 hours
- Anhepatic phase: 40 minutes



Above: Passive porto-jugular shunt placement
Below: Liver implantation: caval, portal, and arterial anastomoses (left to right)



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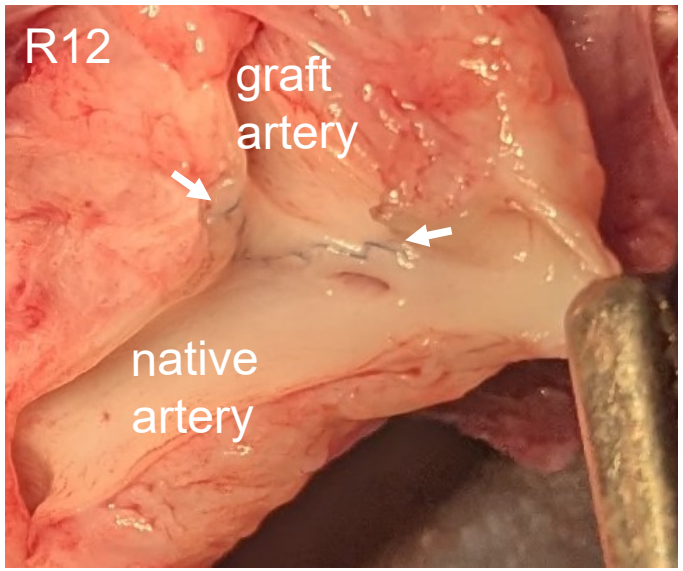
Hepatic artery patency

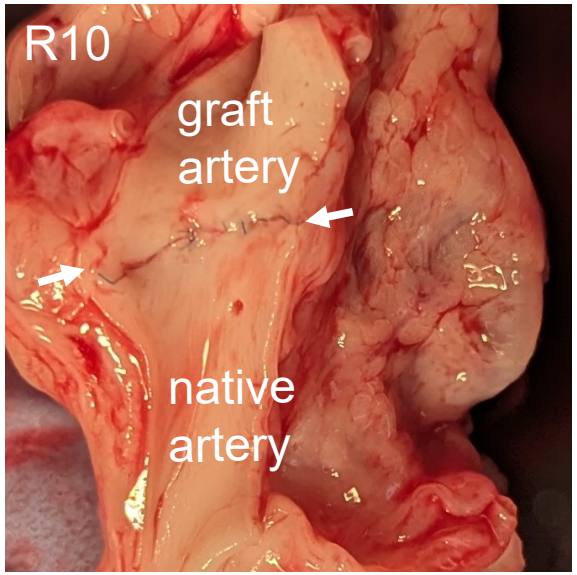
From early findings of jaundiced recipients nearing the end of follow-up, hepatic artery thrombosis was suspected as a possible confounder.

Necropsy findings were initially inconclusive because of the pig's inherent hypercoagulability.

After heparin administration prior to euthanasia no artery thrombosis was observed in any recipient.

Interpretation of these observations is that jaundiced recipients were likely infected. Necropsy and histological findings were consistent with this hypothesis.





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Nanoparticle administration and tolerance

4/10 treated animals received the full 10 doses

Some recipients reacted strongly to IV injections of NPs

- heavy breathing, screams, recovery in 2-5 minutes)

Interpretation remained cautious as reactions to injections occurred in recipients with catheter-related complications (infections) and as reactions were also present during injection of other treatments (e.g. pantoprazole).

No adverse reaction to the NPs was observed since the December meeting.

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Biochemical data

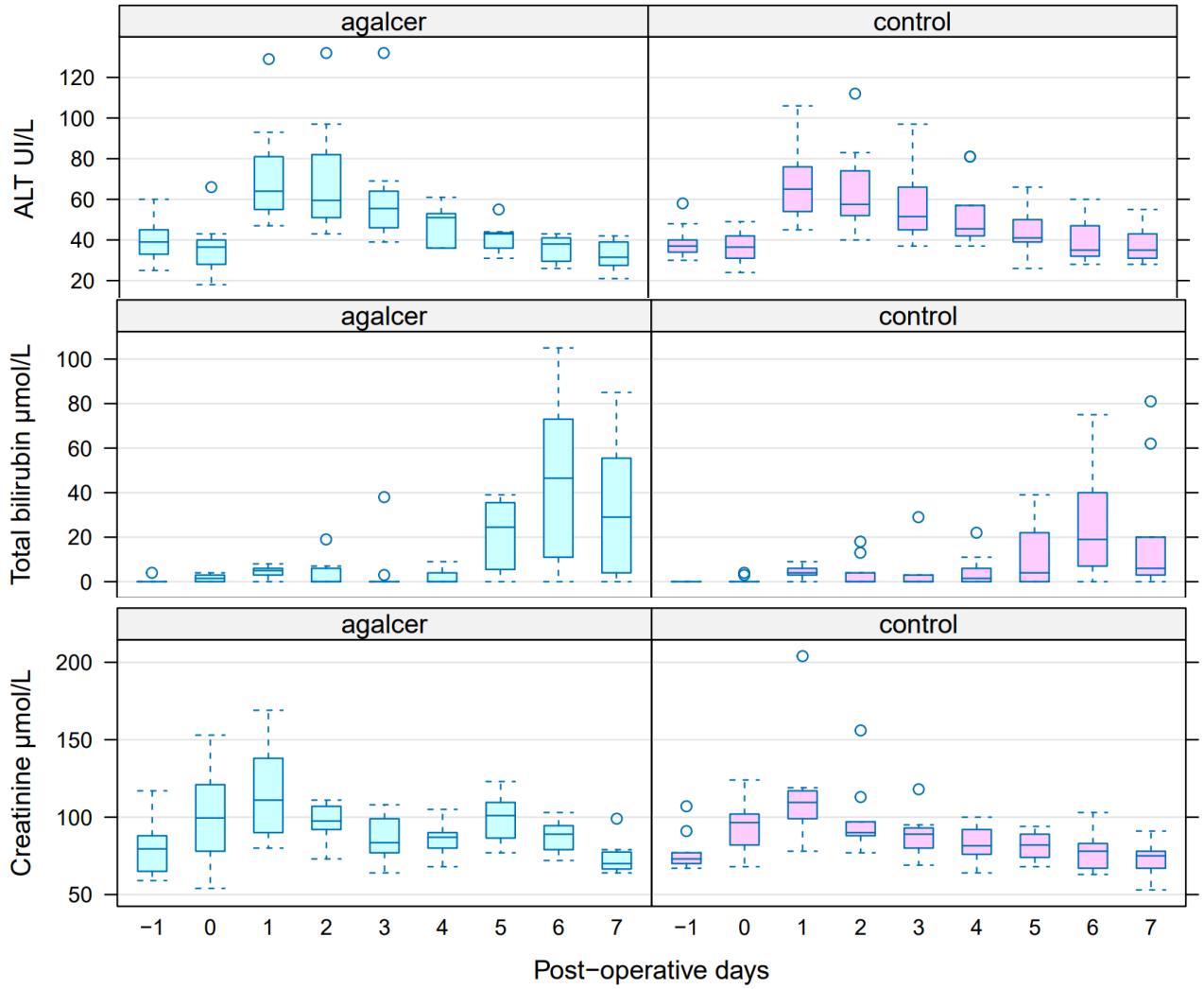
Observed pattern:

- Early variations consistent with liver ischemia/reperfusion during the first post-operative week
- Transient cholestasis
- Normalisation of cholestasis markers in recipients with prolonged survival
- Cholestasis re-appeared near the end of follow-up in infected recipients

No kidney function impairment except a transient post-operative elevation of creatinine values

No observed difference between groups

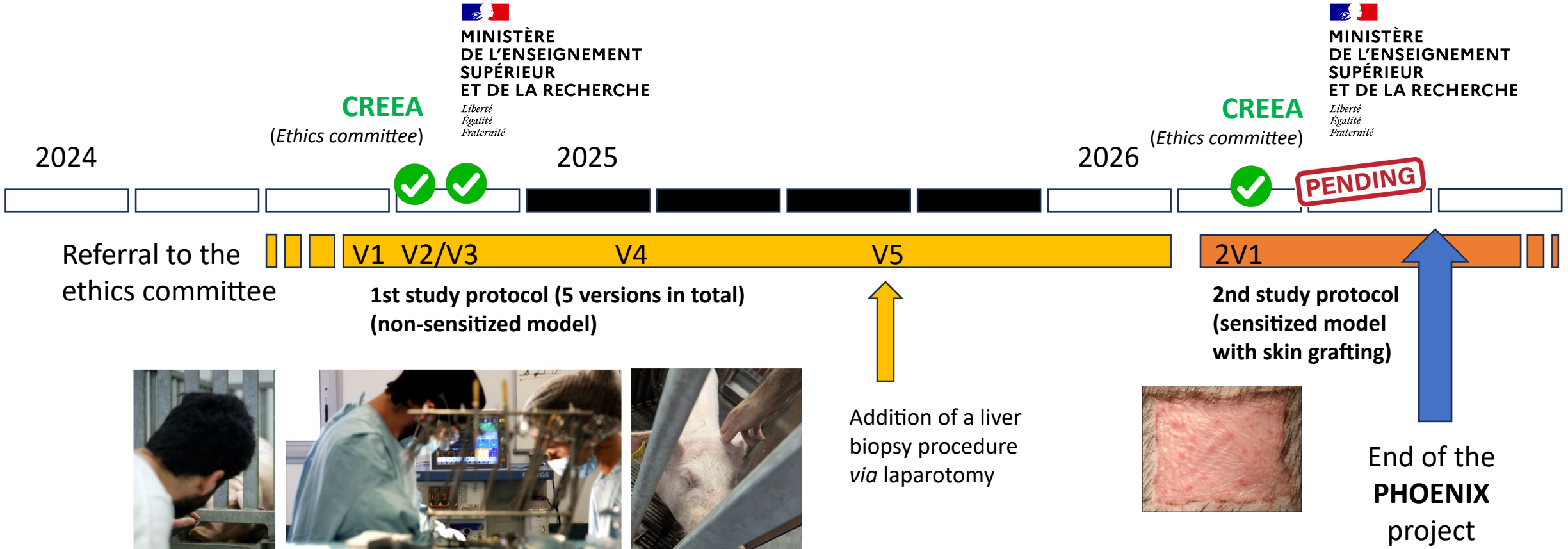
No clear nanoparticle toxicity signal was observed



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Regulatory and ethical procedures for WP3



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Forward focus after RP2

Schedule after RP2:

- Follow-up of the first 20 experiments (completed on June 23)

- Inflammation panel and donor-specific antibody (DSA) detection
- available samples will be processed this summer
- DSA detection by FACS from samples shipped to IRFMN

- Test sensitized model using donor skin graft before liver transplantation using the same experimental plan
- Use T3.2 results as the main mechanistic output if results from T3.1 remain limited

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